“ A Prospective, Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in Patients undergoing Elective Thyroid Surgeries ’’

REG NO: 201220006

Dissertation submitted to

THE TAMILNADU DR. M.G.R.MEDICAL UNIVERSITY

in partial fulfilment for the award of the degree of

DOCTOR OF MEDICINE

IN

ANAESTHESIOLOGY

BRANCH X

INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE

MADRAS MEDICAL COLLEGE

CHENNAI- 600 003

APRIL 2015

CERTIFICATE

SThis is to certify that the dissertation entitled, **" A Prospective, Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in Patients undergoing Elective Thyroid Surgeries "** submitted by **Dr. C.KALAIYARASI** in partial fulfilment for the award of the Degree of Doctor of Medicine in Anaesthesiology by the Tamilnadu Dr. M.G.R Medical University, Chennai is bonafide record of the work done by her in the **INSTITUTE OF ANAESTHESIOLOGY & CRITICAL CARE**, Madras Medical College and Rajiv Gandhi Government General Hospital, during the academic year 2012-2015.

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DECLARATION

I Dr. C.Kalaiyarasi solemly declare that this dissertation entitled **" A Prospective, Randomized Double Blind Study to Compare the Effectiveness of prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in Patients undergoing Elective Thyroid Surgeries "** is a bonafied work done by me in the Institute of Anaesthesiology and Critical Care, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai, during the period of 2012-2015 under the Guidance of **Prof U.G.Thirumaaran,M.D.** Professor of Anaesthesiology , Institute of Anaesthesiology and Critical Care, Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 and submitted to The Tamilnadu Dr. MGR Medical University ,Guindy, Chennai -3, in the partial fulfilment of the requirement for the award of the Degree of Doctor of Medicine in Anaesthesiology.

I have not submitted this dissertation previously to any university for the award of any degree or diploma.

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ACKNOWLEDGEMENT

I am extremely thankful to **Dr.R.Vimala, M.D.,**Dean,Madras Medical College, for her permission to carry out this study.I am immensely grateful to **Prof.Dr.B.Kala, M.D., DA.,** Director and Professor, Institute of Anaesthesiology and Critical Care, for her concern and support in conducting this study.I am extremely grateful to my guide **Prof.Dr.U.G.Thirumaaran,M.D.,** Professor of Anaesthesiology, Institute of Anaesthesiology and Critical Care for his concern, inspiration, meticulous guidance, expert advice and constant encouragement in preparing and doing this dissertation. I am extremely thankful to my professors **Dr.Esthersudharshini Rajkumar, M.D., DA., Dr.S.Ananthappan, M.D., D.A., Dr.Ganthimathi**., **MD., DA., Dr.Samuelprabakaran, M.D., D.A., Dr.Lakshmi, M.D., D.A., Dr.Pangajavalli M.D., D.A.,** Institute of Anaesthesiology and Critical Care, for their constant motivation and valuable suggestions.

I am extremely grateful to my Assistant Professors **Dr.Ganesh, Dr.Suganthalakshmi, Dr.Sivakanth., Dr.Sudakar** for their guidance and expert advice in carrying out this study.

I am thankful to **Mr.Albert Joseph**, statistician who helped me in statistical aspects of my study.

I am thankful to the Institutional Ethics Committee for their guidance and approval for this study.

I am thankful to all my colleagues and friends for their help and advice in carrying out this dissertation.

I am grateful to my family and friends for their moral support and encouragement.

Last but not the least, I thank all the patients and their family members for willingly submitting themselves for this study.

CONTENTS

ABSTRACT

AIM

A Prospective, Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in Patients undergoing Elective Thyroid Surgeries

Key Words: Shivering ,Granisetron, Pethidine, Post operative.

METHODS

This study was approved by institutional Ethical committee of Madras Medical College of Chennai. The study was A Prospective, Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Post operative Shivering in Patients undergoing Elective Thyroid Surgeries. Informed consent obtained from patients regarding study.90 patients randomly allocated into three groups.group P,group G,and group S receives Pethidine, Granisetron and Saline repectively.

RESULTS:

No shivering occurs in Pethidine group 83.3%(n=25), Granisetron 73%(n=22), placebo group27%(n=8) P-value statistically not significant between Granisetron and Pethidine groups but significant($P<0.05$) in placebo group. Shivering occurs at grade 3 in Pethidine group 7%(n=2), Granisetron10%(n=3), placebo group60%(n=18) P-value statistically not significant between Granisetron and Pethidine groups but significant in placebo group($P<0.05$)

CONCLUSION

From this study prophylactic use of both Granisetron and Pethidine were equally effective for the prevention of postoperative shivering. Granisetron also prevents postoperative nausea and vomiting.

INTRODUCTION

Shivering after anaesthesia is the most frequent problem during the early recovery phase of general anaesthesia and during neuroaxial anaesthesia. Incidence of postanaesthesia shivering occurs following general anaesthesia is between 40 – 60%. Postoperative shivering was in 6th position of among 33 low morbidity clinical outcomes[(3)]. The incidence of shivering following general anaesthesia or neuroaxial anaesthesia depends upon the gender, age, room ambient temperature, drugs used and the duration of the procedure. Following anaesthesia shivering is extremely discomfort to patients and can increase postoperative pain. Postoperative shivering also causes several physiological changes such as increased in sympathetic stimulation, increased tissue oxygen consumption and carbondioxide production which results in raised minute ventilation which increased stress on the cardiopulmonary system. Cardiac output and metabolic oxygen

demand is also increased. Metabolic acidosis, oxygen desaturation, and hypoxemia may occur in elderly patients with limited cardiopulmonary reserve. There are number of several studies have been conducted for the pharmacological prevention and management of postoperative shivering. The following drugs are used to treat shivering which are Pethidine, Tramadol, Clonidine, and Ketamine. Among these drugs Pethidine found to be most effective in prevention of postoperative shivering although its action not completely understood. But it may act through kappa opioid receptors[5] directly on the thermoregulatory centre. The study by Alfonsi et[11] al Studies suggested the role of serotonergic system in control of postanaesthetic shivering. Serotonin (5-Hydroxytryptamine) is generally present in the brain and spinal cord, which is biological amine in nature. 5-HT3 receptor antagonist is effective in the prevention of emetic symptoms. Granisetron is a 5-HT3 receptor antagonist. Asif Iqbal[1] and his colleagues conducted a study comparing the prophylactic use of Granisetron 40 microgram/Kg body weight and Pethidine for prevention

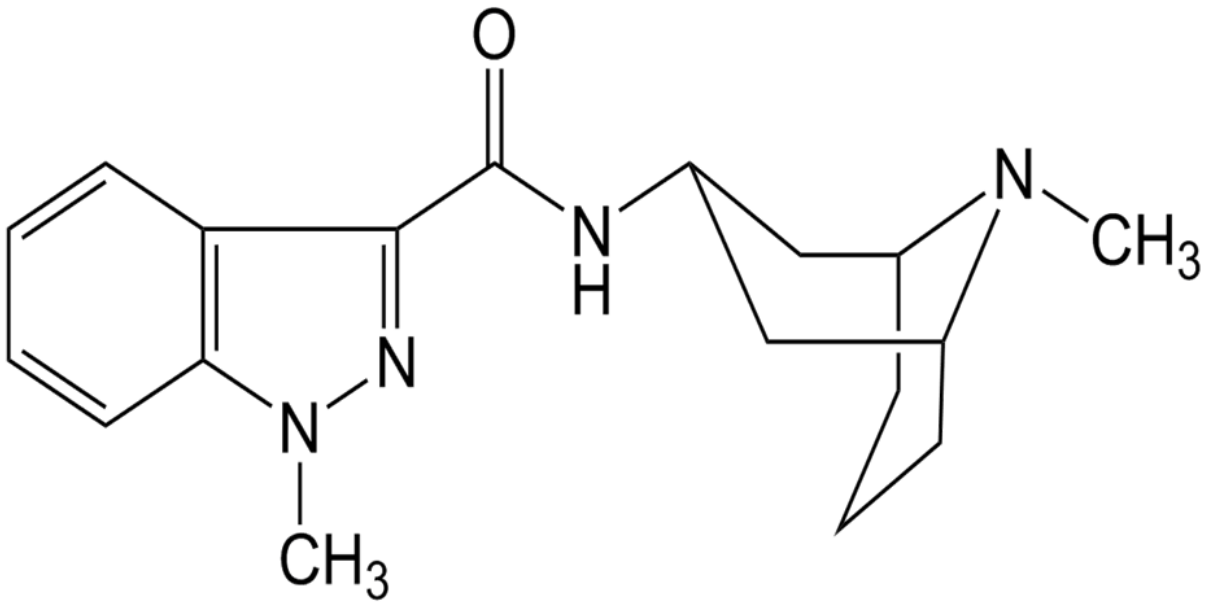
of postoperative shivering in patients undergoing general anaesthesia.

We designed a study in our hospital for the prevention of postanaesthesia shivering following general anaesthesia by Prophylactic use of intravenous injection Granisetron and Prophylactic use of intravenous injection Pethidine and compare the effectiveness of these two drugs for the prevention of postoperative shivering.

AIM OF THE STUDY

To Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in patients undergoing Elective Thyroid Surgeries.

GRANISETRON STRUCTURE



PHARMACOLOGY OF GRANISETRON

Granisetron is a 5HT3 receptor antagonist, clinically used as an antiemetic agent.

DESCRIPTION:

Granisetron is highly selective inhibitor of Type 3 serotonergic receptors or 5-hydroxytryptamine, (5-HT3) receptors. It has little or no action over the other types of serotonin receptors. Granisetron prevents nausea and vomiting induced by chemotherapy and radiotherapy. It has safety profile and well tolerated by the patients and interactions with other drugs very minimal, which makes Granisetron is the drug of choice for elderly cancer patients to prevent vomiting. Granisetron is crytalline solid in nature and white to off-white in colour, which is freely soluble in water and 0.9% sodium chloride at 20°C and it is bitter in taste. Injection Granisetron hydrochloride available in 1mg or 2mg ampoules and as tablet 1mg or 2mg.

MECHANISM OF ACTION

Granisetron is highly selective inhibitor of type 3 serotonergic receptors or -5-hydroxytryptamine,(5-HT3) receptors. Granisetron acts on the release of serotonin from the damaged gastrointestinal mucosa of the enterochromaffin cells following chemotherapy and radiotherapy. 5-HT 3 receptors situated on the afferent vagal nerves and in the brain. The 5-HT 3 receptors are stimulated by serotonin released from the enterochromaffin cells which stimulates the vomiting center in the brain through vagal afferent fibers and produce vomiting. Granisetron blocks the vomiting induced pathway by binding to 5-HT 3 receptors and inhibit serotonin release. 5-hydroxytryptamine may influence both heat production and heat loss pathways. Granisetron action on other types of serotonin receptors are negligible. Other types of serotonin receptors are 5-HT, alpha1, alpha 2, and beta-adrenoreceptors.

PHARMACOKINETICS

ABSORPTION:

Following oral administration Granisetron is completely absorbed and rapidly reaches the peak plasma concentrations in 2 hours. Oral bioavailability is complicated by food, which has high intra-subject and inter-subject variability.

DISTRIBUTION:

Granisetron distributed in the plasma in high concentration. Freely distributed in the plasma red blood cells also present. Volume of distribution is 2-3 L/kg[12] Onset of action is within 1-3 minutes of intravenous administration and which controls emesis. Duration of action is upto 24 hours. Plasma protein binding is approximately 65%. Half-life in cancer patients is upto10 to 12 hours, and 3 to 4 hours in healthy volunteers.

METABOLISM:

In the liver Granisetron is metabolized by various changes such as demethylation and oxidation then end metabolites formed by conjugation, and these metabolites also have some antagonist activity on 5-HT3 receptor.

ELIMINATION:

Clearance of granisetron is predominantly by hepatic metabolism. Metabolites are excreted in the urine and in the feces. Unchanged forms also excreted in the urine.

USES :

Prevention and treatment of

- Chemotherapy and radiotherapy induced acute and delayed nausea and vomiting.
- Post -operative nausea and vomiting.

CONTRAINDICATION:

Hypersensitivity to Granisetron or related substances, or any other ingredient of the preparation.

ROUTES OF ADMINISTRATION:

ORAL: Tablet 2mg/day or 1mg two times per day orally, one hour before cancer treatment either chemotherapy or Radiotherapy

INTRAVENOUS :

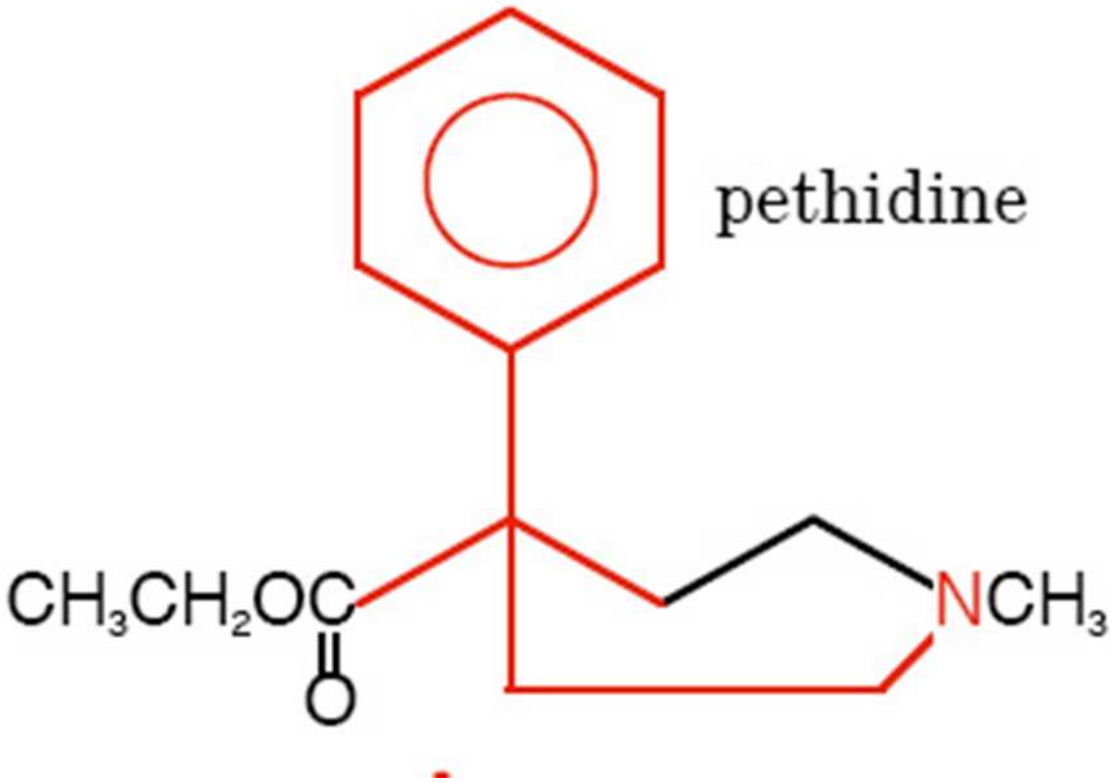
40 µgm/ kg body weight.

Dosage adjustments are not required in hepatic dysfunction renal dysfunction and in elderly patients**.**

ADVERSE REACTIONS:

Side effects	>10%	1% - 10%	<1%
Central nervous system	headache	Asthenia, Dizziness, Anxiety,	Somnolence, Agitation, Weakness
Gastrointestinal system	-	Loose motion , Constipation, and abdominal pain,	-
Haemtological system	-	Blood pressure changes	-
Cardiovascular system		Arrhythmias	
Endocrine / metabolic	-	-	Hot flashes
Hepato biliary system	-	-	Liver enzyme may increase

STRUCTURE OF PETHIDINE



PHARMACOLOGY OF PETHIDINE

Pethidine is a synthetic opioid which is used as an analgesic and for prevention of postoperative shivering. Its actions are similar to Morphine.

Description: Pethidine is available as Pethidine hydrochloride.

STRUCTURE-ACTIVITY RELATIONSHIPS:

The wide array of different molecules that produce morphine like analgesia and side effects. Pethidine is a phenylpiperidine derivative which presents with two rings in structure. First totally synthetic opioid. It has an anticholinergic activity. But was found to have significant analgesic activity. It has moderate affinity for κ- and δ-opioid receptors has well-recognized weak local anesthetic properties. But because of its local anesthetic effects, neuraxial Meperidine may also produce sensory and motor blockade as well as sympatholytic effects. There effects are not seen with other opioids.

PHARMACOKINETICS

Pharmacokinetics of the drug is described by the following four parameters: absorption, distribution, biotransformation, and excretion. Rate of elimination can be measured by clearance.

ABSORPTION:

Oraly administered drug is absorbed well from the gastrointestinal tract.

Morphine is 10 times more potent than Pethidine. Following intramuscular injection Pethidine is absorbed completely into the plasma which reaches peak levels within one hour.

DISTRIBUTION:

Pethidine is moderately lipid soluble, and is 40 to 70% protein bound, mostly to albumin and α_1-acid glycoprotein. Following intravenous administration, pethidine plasma concentration falls rapidly. As the drug is distributed to extravascular sites, including sites of action and non - eliminating tissues. Pethidine's redistribution half-life is 4 to 16 minutes. Terminal elimination half-life is between 3 and 5 hours. The

elimination half-life is not prolonged in elderly patients. In neonates and infants, the median elimination half-life is 8 to 10 hours. Pethidine has a large steady -state volume of distribution in the range of 3.5 to 5 L/kg in adults.

METABOLISM:

Pethidine is mainly metabolized in the liver by biotransformation which is converted into pethidinic acid by a process of hydrolysis and by conjugation with glucuronic acid. Which is converted into norpethidine by N- demethylation. Hepatic blood flow decides pethidine clearance because it has high hepatic extraction ratio. The clearance about 10 ml/kg/min. Pethidine's end products can cause seizure due to central nervous system stimulation.

EXCRETION:

Kidneys mainly removes the end products of Pethidine. Through hepato biliary system about 10% eliminated. Dose should be reduced in renal and hepatic impairment. Urinary excretion may be enhanced by acidification of the urine.

Physicochemical Characteristics and Pharmacokinetics

s.no	Parameter	Pethidine
1	pKa	8.5
2 3	% Nonionized (pH 7.4) water partition coefficient	7 39
4	Protein binding (%)	70
5	Clearance (ml/min)	1020
6	steady-state volume of distribution	305
7	Slow redistribution half-life ($T_{1/2}\pi$, min)	4-16
8	Elimination half-life ($T_{1/2}\beta$, h)	3-5

PHARMACODYNAMICS

Drug action on the body described by the following parameters

1. Mechanisms of action
2. Drug interactions,
3. Structure– activity relationships.

MECHANISM OF ACTION:

Opioid receptors are stereo specific in nature which are situated in the central nervous system , pheripheral and spinal cord at presynaptic and postsynaptic areas. Endogenous ligands are usually binds to opioid receptors. The opioid drugs binds to the receptor on its anionic site and mimics like a ligands following which alter the response of pain pathway. It will reduce the Neurotransmission by increasing potassium conductance and inactivates calcium channel.

EFFECTS OF DRUGS ON DIFERENT SYSTEMS

THERMOREGULATION AND SHIVERING:

Pethidine is unique among opioids in its ability to effectively terminate or attenuate shivering. The effect of antishivering property is due to the reduction of shivering threshold and this activity mediated through the κ-receptor. However the relatively specific κ-receptor agonist nalbuphine did not show significant antishivering activity. Agonist activity at the α_{2B}-adrenoreceptor subtype, suggesting possible action of Pethidine in the antishivering. Alfetanil, Morphine, and fentanyl are not effective as Pethidinee in the prevention of shivering. Tramadol (0.5 mg/kg) suppressed post epidural anesthetic shivering in parturients as effectively as Pethidine (0.5 mg/kg). But the incidence of somnolence was lower with Tramadol than with Meperidine.

CARDIOVASCULAR SYSTEM:

Meperidine will increase the heart rate because Pethidine is structurally similar to atropine.

RESPIRATORY SYSTEM:

Histamine may be released by Pethidine which may cause bronchospasam in susceptible individuals.

ROUTES OF ADMINISTRATION AND DOSAGE:

Dosage depends on patient profile of age, weight, sex, previous exposure to narcotics.

PARENTRAL:

1. Intramuscular 25 to 100 mg, every 3-4 hours.
2. Subcutaneous25 to 100 mg, every 3-4 hours.
3. Intravenous 25 to 50 mg slow IV injection, every 3 to 4 hours.
4. Infusion 300µg/Kg weight/hour.

For pain 10 -100 µg/Kg intravenously, for shivering 12.5-25mg intravenously.

CHILDREN:

Analgesia 50 to 200 µg/ kg body weight intramuscular or subcutaneous. For Preoperative 100 to 200 µg /kg body weight 90 minutes before surgery. The total dose should be 100 mg or less. If patients over 70 years of age dose should be reduced to half of its normal dose.

DOSE CONVERTION:

For analgesic effect of intramuscular Pethidine of 75 to 100 mg is equal to the following drugs:

- 10mg Morphine,
- 200µg Fentanyl,
- 120mg Codeine Phosphate,
- 8 to 10 mg Methadone Hydrochloride.

INDICATIONS

- Short term relief for moderate to severe pain.
- Obstetric analgesia.
- Shivering.

CONTRAINDICATIONS

- Allergic to Pethidine.
- Chronic lung disease with respiratory depression.
- Head injury, raised ICT, brain tumor.
- Arrhythmias like Supra ventricular tachycardias,
- Patients on monoamine oxidase inhibitors.
- Toxaemias of Prgnancy,
- Seizure disorders and tetanus,
- Metabolic encephalopathy and Diabetic coma,
- Alcoholic intoxication,
- Liver failure and
- Renal impairment

ADVERSE REACTION:

RESPIRATORY SYSTEM:

Impairment of respiratory function is the most common side effect of Pethidine.

CENTRAL NERVOUS SYSTEM:

Lightheadedness,

Dizziness ,

Sedation ,

Abnormal feelings,

Dimnised orientation,

Psychological problems.

GASTROINTESTINAL

Nausea and Vomiting,

Abdominal discomfort and constipation.

CARDIOVASCULAR SYSTEM:

Complications are less common

It may increase or decrease blood pressure leads to Hypertension or hypertension respectively, vasodilation, ,heart rate changes either tachycardia or bradycardia.

Dermatological complications are also less common, which are Rash, Pruritus, Urticaria and Erythema.

INJECTION SITE COMPLICATION

Local irritation and induration and fibrosis of muscle tissue with frequent repetition of intramuscular injection.

RENAL:

Retention of urine and with oliguria and anuria.

HEPATOBILIARY SYSTEM:

- Increased biliary tract pressure,
- Coledochoduodenal sphincter spasam.

Neuropsychiatric toxicity.

Additive Potential

OVERDOSAGE

Symptoms:

Bradycardia and hypotension, peripheral cold clammy skin and hypothermia leads to shock. Altered sensorium to coma due to central nervous system depression. Respiratory failure due to depression, skeletal muscles weakness. Apnoea , circulatory collapse, cardiac arrest, respiratory arrest and death seen in severe over dosage. Pneumonia, shock, pulmonary oedema, severe hypoxia and terminal narcosis. If Normeperidine concentration in plasma is more than 0.81 µg/ml patients usually develops seizure .

INCOMPATIBLITES:

Inactive complex formed by Pethidine while mixing with Thiopentone.

Clarity of solution was lost when combine with Aminophylline.

Which also becomes incompatible when combined with following drugs Methicillin sodium, Morphine sulphate, Heparin,Phenobarbitone sodium, Phenytoin sodium, sodium bicarbonate , sodium iodide and alkalis.

INTERACTIONS WITH OTHER DRUGS:

The CNS depressant effects of Barbiturates, chloral hydrate, benzodiazepines increased by pethidine, and analgesic effect of pethidine reduced when given along with these drugs.

Phenothiazines: CNS toxicity hypotension and respiratory depression.

Butyrophenones: The CNS depressant effect of tranquillisers is increasd.

When combined with Monoamine oxidase inhibitors can cause hypertension or hypotension, Excitation, sweating, rigidity and coma.

Phenytoin:

Which increases the toxic metabolites of pethidine and increased CNS toxicity and reduce the analgesic effects.

Pethidine will increase the anticoagulants effects Coumarin or Indandione .

THERMOREGULTION

Body temperature is determined by the relationship between heat production as a product of metabolism and heat loss to the environment. Body temperature is regulated and maintained within narrow limits between 36.7 to 37.5℃ by the adjustment of heat production within the body and heat loss from the body into the environment. Temperature is lowest in the morning and highest in the evening. During sleep there is consistently decreased a 10% to 15% in the basal physiologic metabolic rate, presumably reflecting the decreased activity of skeletal muscles and the sympathetic nervous system.

HEAT LOSS:

Heat loss from the body occurs by the following mechanism of radiation, conduction, convection, and evaporation. Under typical circumstances most heat (~60%) is lost by radiation. Contact with a cooler object and administration of cold intravenous fluids and blood products results in reductions in core temperature due to conductive

losses. The rate of convective loss depends on both the temperature and velocity of air in the environment this mechanism known as the wind-chill phenomenon. The body can eliminate excess heat when the temperature of the surroundings is higher than that of the skin by the mechanism of evaporation. With continued exposure to a warm environment, sweat production may be increased upto 1,500 ml/hour. Two -thirds of the heat loss from the respiratory tract by evaporation.

INTERTHRESHOLD RANGE:

Interthreshold range is a range at which the core temperature will not trigger autonomic response which is a few tenths of a degree Centigrade. This range is bounded by sweating threshold in the upper end and vasoconstriction in the lower end.

GAIN:

The changes in the slope of response intensity in relation to Core temperature defined as the gain of a thermoregulatory response.

MAXIMUM INTENSITY:

The intensity of the response no longer increasing in relation to further deviation in core temperature which is known as maximum intensity.

PHYSIOLOGY OF THE TEMPERATURE REGULATION

Thermoregulatory responses are graded, and each particular response is characterized by a threshold temperature at which it is initiated. In humans normal core temperature regulated tightly within narrow range between 36.7 to 37.1℃. Vasoconstriction in response to cold occurs at 36.5℃ whereas shivering occurs when core temperature drops below to 36.2℃.

There are three components that govern the physiology of thrmoregultion

1.Afferent neural pathway

2. Central regulation

3. Efferent response pathway

Following thermal information core body temperature is maintained within narrow therapeutic range by modulation and integration of these

Components. Behavioral regulation is the most important effector mechanism in conscious patients. Behavioral compensations includes appropriate dressing, environmental temperature modification, assuming positions that oppose skin surfaces, and voluntary movement.

AFFERENT NEURAL PATHWAY:

Thermal sensation received from thermal receptors located in the periphery which are presented both in the central as and peripheral areas. There are two types of themal receptors for warm and cold sensation. Cold signals pass through delta fibres and unmyelinated C fibres transmit the warm signals.Spinal cord are thermosensitive which integrate and modulates thermal inputs from thermal fibers. Through lateral spinothalamic tracts information reach the hypothalamus. shivering response inhibited by nucleus raphe magnus, shivering

response increased by locus subcoerulus neurons. Both of which relays information to hypothalamus from skin. The entire spinal cord must be destroyed for loss of all thermoregulatory responses. Total thermal input to the central regulatory system from several regions of the body each contribute 20% of the input. The hypothalamus and other parts of the brain, spinal cord, deep abdominal , thoracic tissues and the skin surface. According to recent several special thermoreceptors were present in the skin and dorsal root ganglia. Special receptors are transient receptor potential,vanilloid ,and menthal receptors which are thermosensitive.Transient receptor potential,vanilloid are activated by heat, menthal receptors are activated by cold.

CENTRAL CONTROL

Body temperature is regulated by the feedback mechanisms of the anterior hypothalamus that are operated predominantly through preoptic nucleus .

1.The anterior hypothalamus-

preoptic region is an important central regulator,

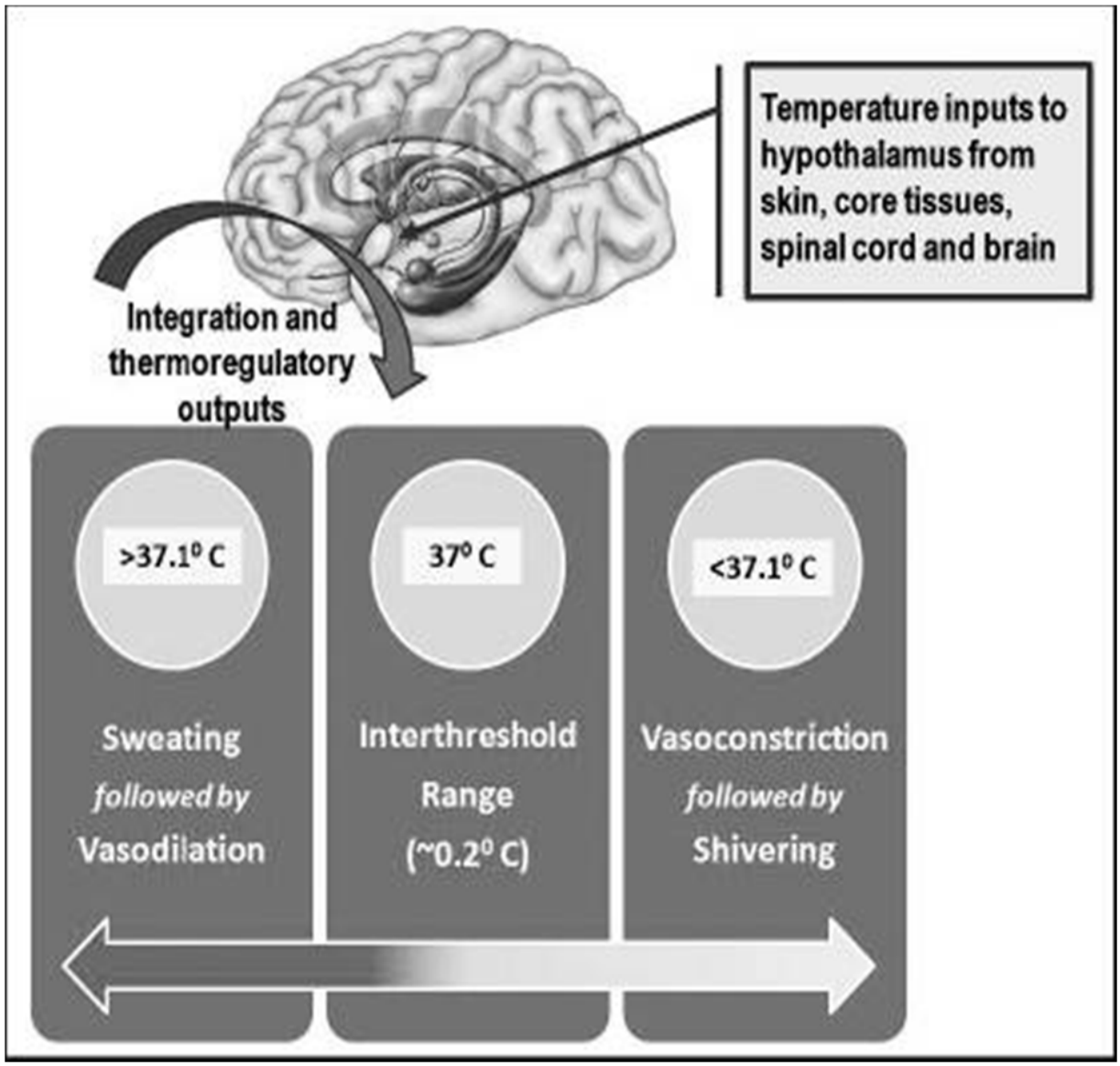
2. Brainstem also subserve this function

3.Spinal cord. The thermostat warm neurons of hypothalamus detects body temperature changes and compare the triggering core temperatures thresholds of afferent pathway. Then integrates this information and initiates thermo regulatory responses which are autonomic, somatic, and endocrine responses when the various set points are reached. The Anterior hypothalamus controls the information received from the central structures. Posterior hypothalamus controls the behavioural responses. Information from the skin surface reach the posterior hypothalamus.The effector responses are different according to their interthreshold temperature. Serotonin,acetylcholine and prostaglandin modulates the inhibitory potentials of hypothalamus.Threshold temperatures are changed daily in cyclical pattern known as circadian rythm variation between 5 to 1^0 C and The interthreshold range is between 0.2 to 0.4^0C which is0.3 to 0.5^0C higher in women than men. The shivering threshold is poorly regulated in the elderly.

EFFERENT RESPONSE PATHWAY

Common efferent pathway achieve optimal thermoregulation through integration of multiple inputs from afferents in an orderly fashion. Efferent responses are either increase heat loss or promote heat gain based on thermal disturbances Each response is governed by a specific threshold.The principle protective mechanisms against hypothermia includes, Thus shivering is the “last resort” of activity following hypothermia. The body temperature to be maintained at a value for optimum enzyme activity for a constant rate of metabolism, optimal nervous system conduction, and skeletal muscle contraction.

cold response below 36.5^0C	Warm response above 37.5^0C
Vasoconstriction Shivering Non Shivering	Vasodilation Sweating



NONSHIVERING THERMOGENESIS:

Brown fat produce heat by cellular metabolism without muscle activity which is known as chemical thermogenesis or nonshivering thermogenesis. Sympathetic nervous system stimulates heat production by circulating Catecholamines without increasing mechanical work. Which has been demonstrated in infants. The Chemical thermogenesis can increase the rate of heat production by as much as 200% in infants Shivering is not well developed in newborn infants.

SHIVERING THERMOGENESIS:

Initially core body temperature is increased by behavioral response, vasoconstriction and peripheral arterio-venous shunting of blood.When these measures failed shivering is last response to generate heat by increasing muscular activity. The vasoconstriction threshold is an entirely 1^0 C more than the shivering threshold. Decreased core temperature can cause shivering by which to increases the body heat production. The posterior hypothalamic area responsible for the response to hypothermia.

PHYSIOLOGY OF SHIVERRING

1. Thermoregulatory response due to hypothermia,

2. Inflammatory response due to release of cytokines,

3. Loss of autonomic thermoregulatory functions,

4. Postanesthesia shivering.

DEFINITION

Shivering is defined as, spontaneous, , oscillatory and an involuntary mechanical activity of skeletal muscle associated with an increased oxygen consumption by 600% [19] above the baseline .

CLASSIFICATION

Depending on the thermoregulation shivering is are classified into two **Types:**

1.Thermoregulatory and

2.Nonthermoregulatory in nature.

THERMOREGULTORY SHIVERING :

In hypothermia Shivering occurs for heat production to maintain normothermia if vasoconstriction response is inadequate.

NON THERMOREGULTORY SHIVERING:

Non thermoregulatory shivering in normothemic individuals includes

1. Pain after surgery,
2. Endogenous pyrogens release,
3. Uninhibited spinal reflexes,
4. Adrenal suppression and
5. Labour and delievery.

RISK FACTORS:

1. Male gender,
2. Prolonged surgeries and ,
3. Anaesthesia,
4. Younger age groups.

GRADING OF SHIVERING :

Shivering scale validated by Tsai and Chu

The intensity of postanaesthesia shivering graded according to the involvement muscle groups ,severity of shivering grded from Grade 0 to Grade 4.

GRADES:

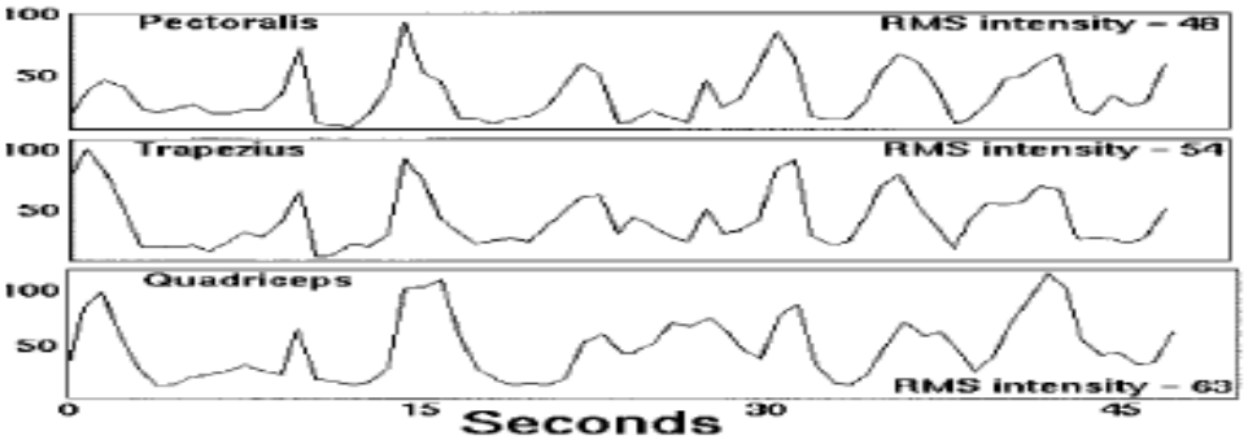
0	No shivering activity,
1	Only piloerection and vasoconstriction,
2	Involving only one muscle group,
3	More than one muscle group but no generalized shaking
4.	Generalized the whole body involved.

PATTERNS OF SHIVERING:

According to the nature of shivering which is classified into two patterns. General anaesthesia has two patterns of shivering and also confirmed of EMG assessment.

FIRST PATTERN:

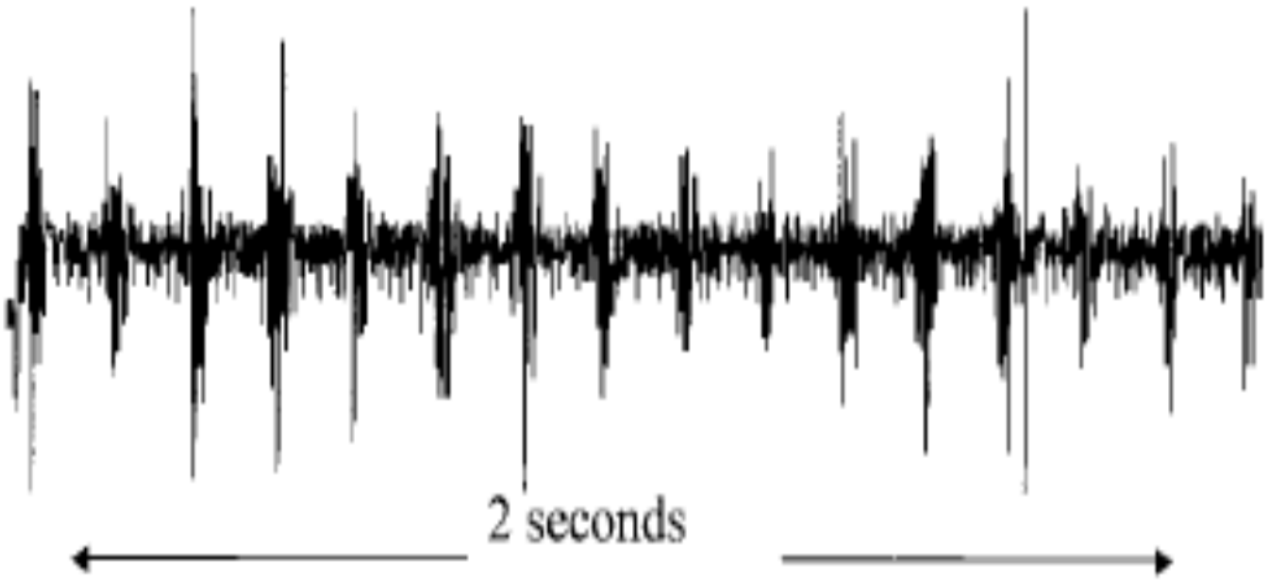
Seen in Thermoregulation shivering as a synchronous ”waxing and waning” pattern.and frequency is about 4 to 8 cycles per min and which is tonic in nature.this patterns also seen volunteers who exposed to cold enviroments.



EMG –TONIC –PATTERN SHIVERING

SECOND PATTERN:

Shivering is clonic in nature at frequence rate of 5-7Hz. As seen in spinal cord transection with uninhibited spinal reflexes. Also seen in a study of isoflurane with 0.2-0.4 end-tidal concentration.



EMG – CLONIC-PATTERN SHIVERING

MECHANISM OF SHIVERING

The shivering motor centre situated in the posterior hypothalamus is stimulated when the temperature of Preoptic areas is very cool. Temperature changes produced in neuronal activity in mesencephalic reticular formation and dorsolateral pontine and medullary reticular formation by effector pathway of shivering descends from the posterior hypothalamus , and muscle tone increasd by α motor neurons common pathway. shivering occurs when muscular activity is increased. Through renshaw cells, a group of inhibitory interneurons mediate the shivering by recurrent inhibition. Three compensatory defence mechanisms to counter hypothermia and prevent subsequent heat loss by the following

1. Vasoconstriction,
2. Heat production without shivering,
3. Heat production by muscle shivering.

Skeletal muscle shivering is one of the mechanism that, can be treated and can be prevented.

PREVENTION OF POSTOPERATIVE SHIVERING:

Shivering can be prevented by two methods

1. Non Pharmacological
2. pharmacological by drugs

PREVENTIVE MEASURES:

The dictum is always prevention[3]is better than cure. This dictum can be applied for prevention of postoperative shivering. Most authors also suggested the importance of prevention of hypothermia during surgery.

NONPHARMACOLOGICAL :

Increasing the skin temperature and decreases the temperature gradient between the central and peripheral compartments by the following methods ,such as increase the operation room ambient temperature,

Which prevents external cooling of the body, Preventing heat loss from the body by convective mechanism of heat loss which can be done by insulation methods like external warming with cotton blankets and use of warm skin disinfectant. Internal warming with use of warm intravenous fluids and warm Local anaesthetics for neuraxial blockade. These measures increase the skin temperature without change in core body temperature and prevents internal heat redistribution. During anaesthesia intra compartmental heat changes due to vasodilation which heat transfers from periphery to central than postoperative warming for the prevention of postoperative shivering. Cutaneous loss can be prevented by insulation method which prevents about thirty percent. By all these measures core temperature should be maintained more than 36°C.

PHARMACOTHERPY:

Several drugs are used for the prevention of shivering.

MECHANISM OF ACTION

For the prevention of shivering central thermoregulatory mechanisms should be modulated and modifying shivering adaptive threshold. when core temperature decreased 5-HT induce shivering and vasoconstriction which leads to increase core temperature. Adaptive mechanism modification responded to the balance between 5 HT and Noradrenaline. By inhibit the synaptosomal uptake of 5-HT and Noradrenaline prevent shivering .Shivering and vasoconstriction induced by Acetylcholine and nicotine. When preoptic area is cooled the Acetylcholine release is increased to about 88[(3)] percent. During warming Acetylcholine release[(3)] is suppressed to 80 percent.

The following drugs are used for prevention of shivering

1. Pethidine - κ receptor agonist**,**
2. Tramadol – opioids ,
3. Clonidine -central α2 –adrenergic agonist,
4. Ketamine - N-methyl-D- aspartate receptor antagonists ,
5. Magnesium sulfate-physilogical NMDA receptor antagonists,
6. Physostigmine - centrally acting cholinesterase inhibitor,
7. Granisetron -5HT3 antagonist.

TEMPERATURE MONITORING

Human body temperature is heterogeneous in nature, core temperature is always higher than peripheral temperature the difference between 2 to 4^0C. Deeper structures are always warmer than peripheral structures. Temperature monitoring is very much important for prevention of hypothermia before onset of shivering. Skin temperature usually varies. Measure of Core temperature is the gold standard for temperature monitoring.

MONITERING SITES FOR CORE TEMPERATURE:

1. Tympanic membrane,
2. Pulmonary Artery,
3. Nasopharynx,and
4. Oesophagus distal part.

NEAR CORE TEMPERATURE SITES:

Mouth, Axillae, Bladder, Rectum and Skin surface. Each site and modality of monitoring has its own limitations, which should not exceed 0.5^0C level of inaccuracy.

METHODS OF MEASUREMENT :

1. Most accurately measured by Infrared Thermometers and which are inexpensive.

2. Tympanic probes are being soft and pliable. Disadvantages are risk of perforation, and incorrect position.

3.Oesophageal probes incorporated into oesophageal stethoscopes which are safe and accurate when positioned into the distal Oesophagus.

4. Nasopharyngeal probes are best placed a few centimetres distal to the nares adjacent to the Nasopharyngeal mucosa. Risk of epistaxis when trauma occurs during insertion.

Oral, Axillary, Bladder and Rectal Temperature can measure Core Temperature with fair accuracy in the absence of extreme temperature disturbances.

MECHANISM OF HYPOTHERMIA UNDER ANAESTHESIA

1. Thermoregulation impairement during anaesthesia,
2. Heat redistribution from the core to pheriphery
3. Lower ambient temperatures,
4. Cold intravenous fluids,
5. Heat loss from surgical sites.

GENERAL ANAESTHESIA:

The defence mechanisms of thermoregulation is impaired resulting in heat redistribution from core to the peripheral areas which leads to hypothermia.

During general anaesthesia core temperature changes occur in three phases.

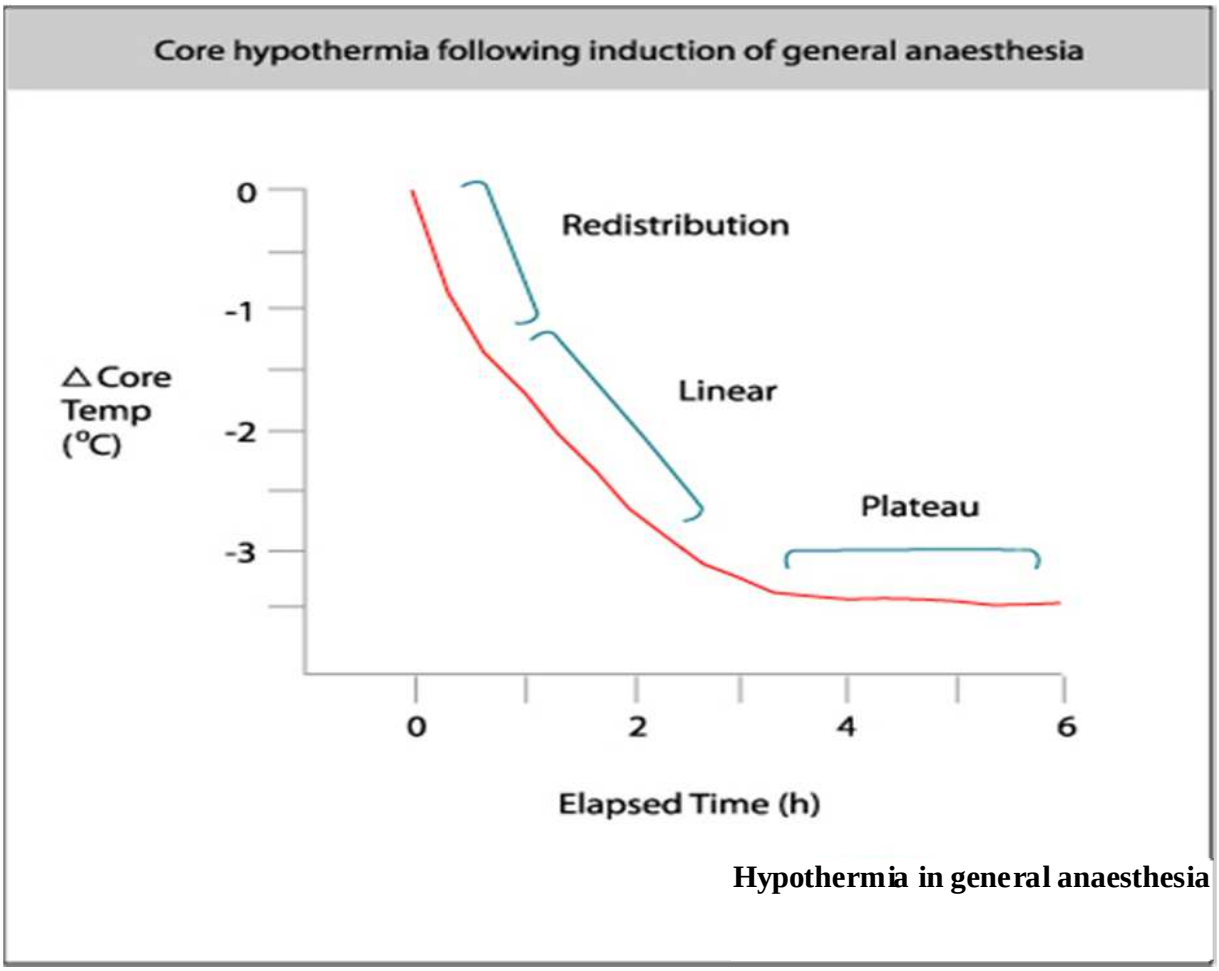
Phase 1- Rapid fall in core body temperature occurs during the first hour of anaesthesia from 1-2^{0}C due to heat redistribution.

Phase 2- Next 3-4hrs the core temperature fall is gradual due to the environment heat loss.

Phase 3- Following phase -2 an equilibrium achieved between heat loss and production.

General anaesthesia the interthreshold range increased from 0.2 – 0.4^{0}C due to thermoregulation impairment which limit the thermal defence responsiveness. After extubation interthreshold range is return to

normal which cause normal thermoregultory response to hypothermia and cause shivering.



Hypothermia in general anaesthesia

Thermoregulation thresholds in unanaesthetised and anaesthetised humans.

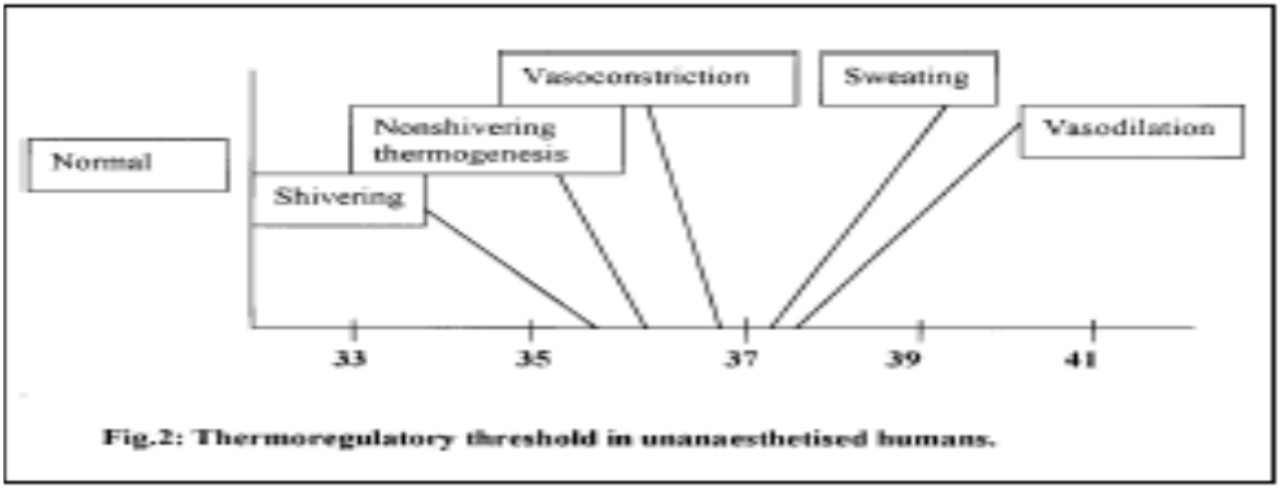


Fig.2: Thermoregulatory threshold in unanaesthetised humans.

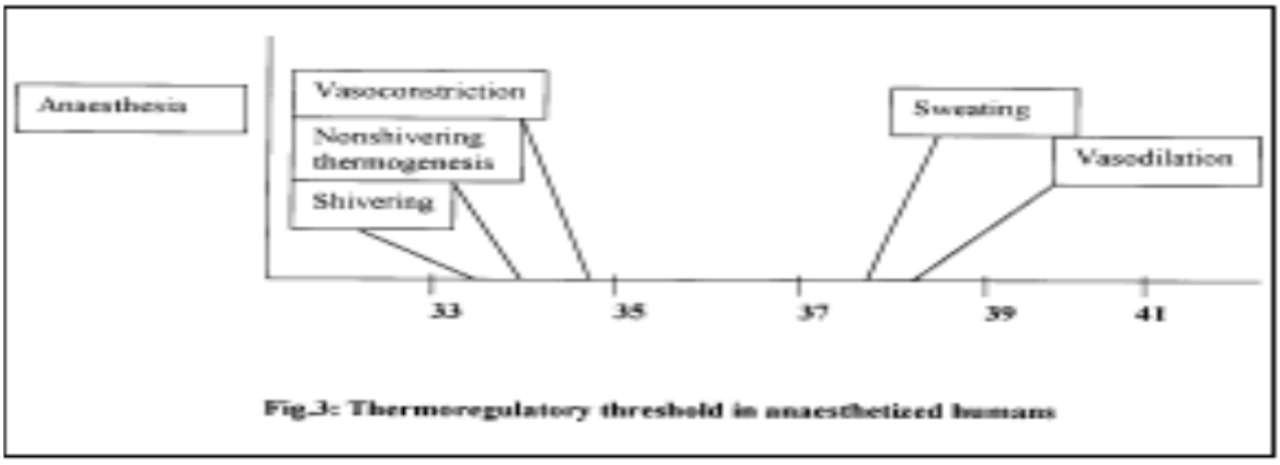


Fig.3: Thermoregulatory threshold in anaesthetized humans

NEURAXIAL ANAESTHESIA:

Above the level of the Neuraxial blockade vasoconstriction and shivering occurs due to thermal defence mechanism. Inadequate in generating metabolic heat as the muscle mass cephalad to the block is small. Similar mechanisms surround with the

Phase 1 - Fall in core body temperature due to internal heat redistribution by vasodilatation .

Phase 2- continuous heat loss occurs thermoregulatory centre is sensed by the normal unblocked area.

Hypothalamus sensed by the elevation of skin temperature above the blockade area which results in altered perception of temperature results in decreasing shivering threshold below the blockade area. Vasodilatation produce ongoing heat loss at below the level of the blockade which results in risk of undetected hypothermia until shivering occurs. Shivering threshold in epidural anaesthesia being directly related to the number of dermatomes blocked. Sacral nerve roots spared which results in reduced thermal afferent input and shivering threshold. In

Spinal anaesthesia associated with complete motor blockade. The difference between these will be postulated that the epidural and intra thecal space differ in terms of thermo receptors and their respective sensitivity.

ADVERSE EFFECTS OF SHIVERING

1.Patient discomfort also has several deleterious effects.

2. Difficulty with monitoring techniques.

3.Increased oxygen consumption and metabolic demand.

4.Increased introcular and intracranial pressure.

5. Metabolic acidosis.

6. Increased carbon dioxide production.

7.Increased post-operative pain from surgical incision stretching.

8.Increased in cardiac output.

9. Increased minute ventilation and systemic vascular resistence

10.Raised plasma catecholemine levels .

Post anaesthesia shivering is predominantly thermoregulatory in nature as a result of the anaesthetic induced inhibition of thermal defense mechanisms and subsequent hypothermia.

HYPOTHERMIA:

Is a core temperature greater than one standard deviation below mean core temperature for that mammal under resting conditions. Mild hypothermia is defined as a core body temperature of between 33.0 – 36.4^{0}C, at which cellular and tissue dysfucntion may develop.During periods of cerebral or cardiac ischaemia, it is thought that hypothermia maybe protective on the basis on decreased metabolic demand,however hypothermia should be considerd in anaesthesia, depends on the risk benefit ratio.

Adverse effects of Mild hypothermia

1. impaired immunity and surgical site infection,
2. delayed wound healing,
3. coagulopathy,
4. increase in allogenic blood transfusions,
5. delayed post anaesthetic recovery,
6. prolonged hospitalistion,
7. patient discomfort, and
8. morbid myocardial outcomes
9. secondary to increased plasma catecholemines.

REVIEW OF LITERATURE

1.Asif Iqbal ,et.al[1]

in 2009 conducted a study to compare the effectiveness of the drugs Pethidine and Granisetron for the prevention of postoperative shivering in patients undergoing laparoscopic surgery under general anaesthesia.90 patients aged 20-60yrs, ASA /PS I and II, they were randomly allocated to three groups receive either normal saline S as negative control, Pethidine 25mg as positive control or Granisetron 40µg/kg intravenously before induction. Nasopharyngeal temperature was measured throughout the procedure. An investigator blinded to the treatment group, graded postoperative shivering in a scale of 0 to 4. In this study, they found that Granisetron 40 microgram /kg was as effective as inj.Pethidine 25mg in preventing shivering after general anaesthesia.

2.D. Dal,et.al [2]

In 2005 done a study to compare the efficacy of low-dose prophylactic Ketamine with that of Pethidine or placebo for the preventing of postoperative shivering in patients undergoing general anaesthesia. A prospective randomized double-blind study enrolled 90 ASA I and II patients undergoing general anaesthesia. Patients were randomly allocated to three groups each groups enrolled 30 patients randomly receive normal saline , Pethidine 20 mg or Ketamine 0.5 mg/ kg drugs were given intravenously 20 min before completion of surgery In their study, none of the patients shivered after prophylactic Pethidine. In this study, they found no difference between the efficacy of Ketamine and Pethidine in preventing postanaesthetic shivering.

3.Masood Entezariasl,et.al [22]

In 2012 this double-blind clinical trial study was carried out on 120 patients who were posted for surgery under general anesthesia. The patients were randomly divided into three groups. Induction and

maintenance of anesthesia for all patients were similar. Temperature of patients was measured every 5 min interval. After induction, saline0.9%, Dexamethasone and Pethidine were injected to groups a, b, and c respectively. In recovery, patients were controlled for visible shivering. Considering the fact that injection of dexamethasone after induction of anesthesia has been able to reduce the postoperative shivering from 47.5% to 10%, and reduction of postoperative nausea and vomiting in the use of the drug, dexamethasone can be used as an alternative to administration of pethidine particularly in patients with hemodynamic instability.

4. **BY JEAN-DENIS ROY,M** [23]

In 2004 volume 3, issue 6 of Anesthesiology Rounds endeavours explained postoperative shivering pathophysiology and discussed preventive strategies and treatments. postanesthesia shivering may not just be a thermoregulatory reaction .Shivering may be one manifestation of an inflammatory response. Powell and Buggy studied Ondansetron, a 5-HT3 antagonist and found that an intravenous dose of 8 mg a just

prior to the induction of general anesthesia significantly reduced the incidence of postoperative shivering. This effect is probably due to a central inhibitory mechanism, given that there was no measurable effect on heat redistribution. These observations suggest that the serotoninergic pathways play a significant role in the regulation of postoperative shivering.

5.Dr. Pradip K. Bhattacharyaet.al[3]

In 2003 reviewed The physiology of PAS, organisation of the thermoregulatory mechanism, various measures for prevention and the methods both pharmacological and non pharmacological, of effective managements in this article. In homeothermic species, a thermoregulatory system coordinates defenses against environmental temperature to maintain internal body temperature within a narrow range Since shivering is an accompanying part of general and regional anaesthesia and it leads to various consequences and discomfort to the patient, proper steps must be taken for its prevention and treatment. The

most effective measures for prevention and treatment are forced air warming and fluid warming. The pharmacological agents for combating it are Nefopam, Tramadol, Physostigmine, Morphine, Fentanyl, and Pethidine etc.As the dictum says, “prevention is better than cure”it holds true for shivering also and it should be practiced.

6.M Entezari Asl, et.al

In 2008. at Alavi University Hospital ofArdabil . They conducted study to see Effect of Ondansetron in Prevention of Postoperative Shivering after General Anesthesia in Gynecological Surgery they selected all patients were in ASA physiologic class I or II. They were randomly selected to receive either 4 mg ondansetron, 0.4 mg/kg Meperidine or 2ml normal saline 2 minutes before inducting anesthesia. They monitored temperature through tympanic membrane. They were observed for shivering. At the end of study they suggested that using Ondansetron instead of Meperidine is better because of its ability to reduce shivering from 50 to 13.3% in addition to reduce vomiting and lower side effects especially in patients with homodynamic instability.

7.H. Alex Choi et.al

In 2010 they conducted the study of aggressive temperature control method The Columbia Anti-Shivering Protocol for Prevention of Shivering During Therapeutic Temperature Modulation to avoid the negative consequences of many anti-shivering therapies. They have developed a stepwise protocol that emphasizes use of the least sedating regimen to achieve adequate shiver control. Methods all patients treated with temperature modulating. At the end of study they concluded that significant proportion of patients undergoing temperature modulation can be effectively treated for shivering without over-sedation and paralysis. Patients at higher risk for needing more interventions are younger men with decreased body surface area.

METERIALS AND METHODS

This study was approved by institutional Ethical committee of Madras Medical College Chennai. The study was A Prospective Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Post operative Shivering in Patients undergoing Elective Thyroid Surgeries. Informed consent obtained from patients regarding study.

INCLUSION CRITERIA:

- Age : More than 18 years
- Weight : 40 -70Kg
- ASA : I and II
- Surgery :Elective Thyroid surgeries
- Who have given a valid informed consent
- Duration of surgeries less than 3 hours

EXCLUSION CRITERIA:

Not satisfying the above said inclusion criteria

- Patients with cardiopulmonary diseases
- Psychiatric diseases
- Patients who require blood or blood products

INFORMED CONSENT:

Before enrolment all the patients were explained about the nature of the study fulfilling selection criteria and the intervention after that informed written consent obtained.

METHOD OF COLLECTION OF DATA:

The patients satisfying inclusive criteria were explained in a detailed manner about the study and procedures and expected side effects. After that informed written consent obtained from the patients. They were clinically reassessed. Age, sex, height, and weight were noted. Baseline vitals like pulse, blood pressure, were noted. Blood sugar, complete blood count, blood urea, serum creatinine, bleeding time,

clotting time, ECG, and chest X-ray were cheked. Airway assessment done then all systems were thoroughly examined.

MATERIALS REQUIRED:

Nasopharyngeal Temperature probe,

Drugs: InjPethidine , Inj.Granisetron., Inj.Glycopyrrolate,

Inj.Fentanyl, Inj.Thiopentone sodium,

Inj.Atracurium Besylate, Normal Saline,

Sevoflurane, and Emergency drugs.

MONITORS:

ECG, SPO_2, NIBP, $ETCO_2$ and Temperature Probes.

RANDOMIZATION:

90 Patients were randomly allocated into three groups – group P,

group G , group S in each groups thirty patients were selected

Group P (n=30) patients were given Inj.Pethidine 25 mg intravenously 5 minutes before induction of general anaesthesia.

Group G (n=30) patients were given Inj.Granisetron 40µgm/Kg intravenously 5 minutes before induction of general anaesthesia.

Group S Placebo (n=30) patients were given Normal Saline intravenously 5 minutes before induction of general anaesthesia.

PRIMARY OUTCOME MEASURES:

- Post operative shivering score
- Temperature , (Core and peripheral),
- Systolic blood pressure,
- Diastolic blood pressure,
- Mean Arterial Pressure ,
- Heart rate and
- SPO_2

Changes during intra operative and post operative period.

SECONDARY OUTCOME MEASURES:

- Post operative Pethidine requirement,
- Nausea
- Vomiting
- Tachycardia / Bradycardia
- Hypotension
- Desaturation

PROCEDURE:

After the nil per oral confirmed, Monitors ECG, NIBP, Pulse oximetry are connected, Nasopharyngeal Temperature probes, Surface Temperature probes were applied after application of lignocaine gel. Base line parameters were noted. Patients were started with crystalloids after intravenous line secured with appropriate intravenous cannula. Heart rate, Temperature (Core and peripheral, OT),

Noninvasive blood pressure (SBP,DBP,MAP) and SPO_2 were noted.

Then study drug were given intravenously 5 minutes before Induction of anaesthesia all the patients were monitored intra operatively and after extubation in the recovery room, for 30 minutes patients received oxygen through facemask. The patients were observed for shivering, pain, nausea and vomiting of the study drug. Heart rate, non-invasive blood pressure, oxygen saturation and nasopharyngeal temperature were measured and recorded on admission to the recovery room at 15 and 30 minute interval. The shivering was graded and side effects were recorded.

Patient with nausea and vomiting were treated with Metoclopramide 10mg slow IV.

Shivering grade 3 or more treated with Pethidine 25 mg intravenously.

Grading of shivering was done by scale validated by Tsai and Chu

GRADES:

- 0 - No shivering,
- 1-Piloerection ,no visible shivering,
- 2- Muscular activity in only one group,
- 3- Muscular activity in more than one group but not generalised
- 4- Shivering is generalised involving whole body.

STATISTICAL ANALYSIS

All parameters were analysed using SPSS 20.0 for windows. These data were compared among three groups using one way ANOVA. The incidence of shivering and side effects were compared using Chi-Square test. The data comparison within the groups were analysed using Bonferroni´s post-hoc testing. The data was expressed as mean ± standard deviation

A P value <0.05 was considered statistically significant.

A P value >0.05 was considered statistically insignificant.

OBSERVATION AND RESULTS

A Prospective, Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in Patients undergoing Elective Thyroid surgeries. The study was conducted in 90 patients. All were female. All the patients completed the study.

There was no difference between the three groups with respect to age, sex, height, weight and procedure. The P value was insignificant

For age (P-0.83), for height (P-0.47), for weight (0.16).These values shown in following tables.

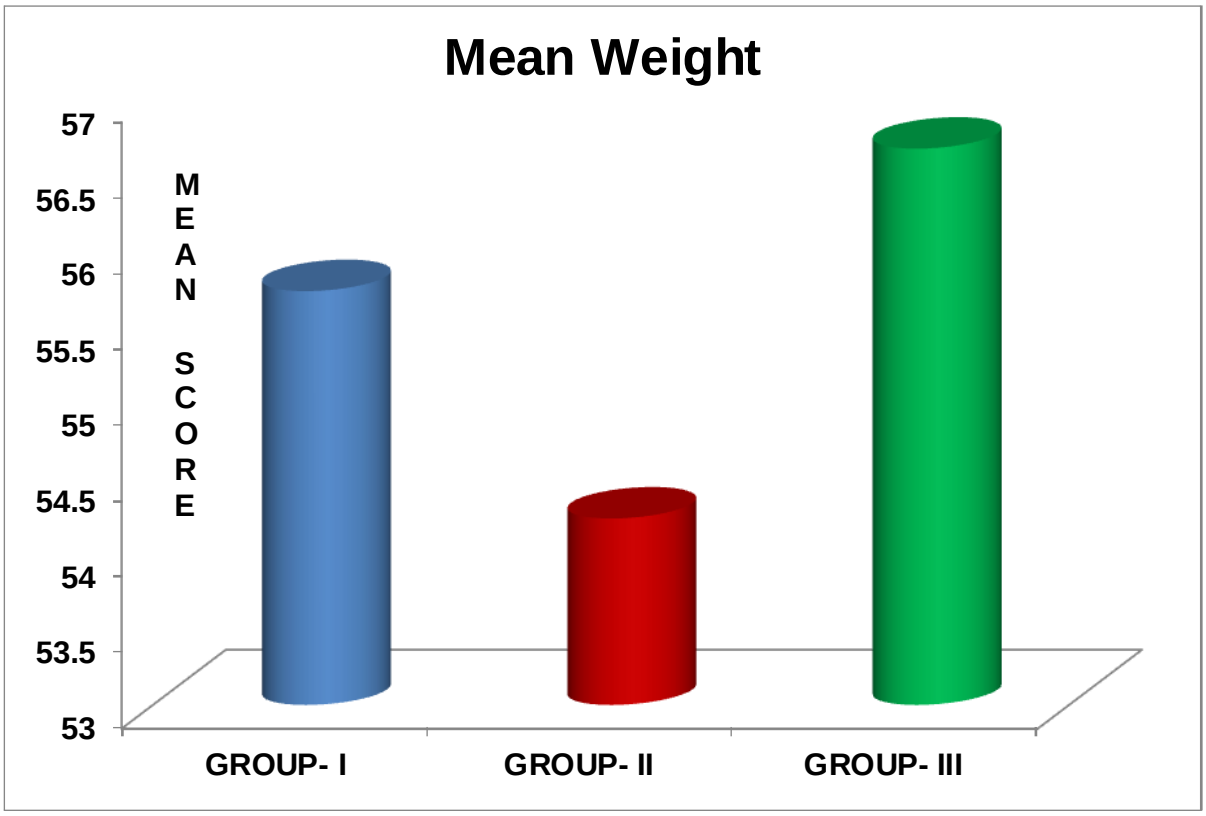
DEMOGRAPHIC PROFILE

TABLE- 1 **Weight (in Kgs)**

Group	Mean	Standard Deviation
GROUP-I	55.73	5.36
GROUP-II	54.23	3.72
GROUP- III	56.67	5.47
F-value	1.87	
p-value	0.16- Not Significant	

TABLE-2 Height (in centimeters)

Group	Mean	Standard Deviation
GROUP-I	154.57	3.36
GROUP-II	154.10	3.69
GROUP- III	155.23	3.60
F-value	0.77	
p-value	0.47	
Significant	Not Significant	


Mean Weight
57
56.5
56
55.5
55
54.5
54
53.5
53
MEAN SCORE
GROUP- I
GROUP- II
GROUP- III

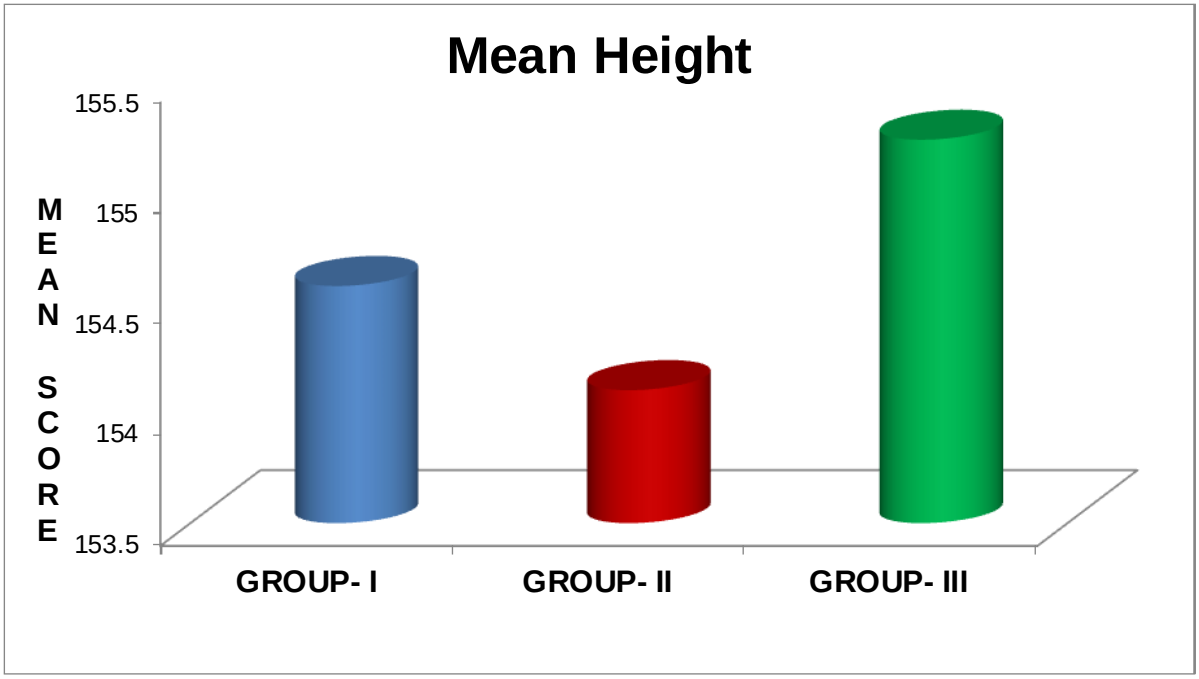

Mean Height
155.5
155
154.5
154
153.5
MEAN SCORE
GROUP- I
GROUP- II
GROUP- III

TABLE-3 MEAN AGE (in years)

Group	Mean	Standard Deviation	Range
GROUP-I	46.87	9.94	22 - 60
GROUP-II	45.83	7.92	32 - 59
GROUP- III	45.47	9.41	26 - 59
F-value	0.19		
p-value	0.83 - Not Significant		

BASE LINE VITALS:

Base line vitals of three groups were compatible . The P-values of Heart rate, SBP, DBP, MAP, and SPO_2 were insignificant between three groups**.** These values are shown in following tables. The P value of Heart rate, SBP, DBP, MAP, and SPO_2 were 0.45, 0.14, 0.07, 0.15 respectively.

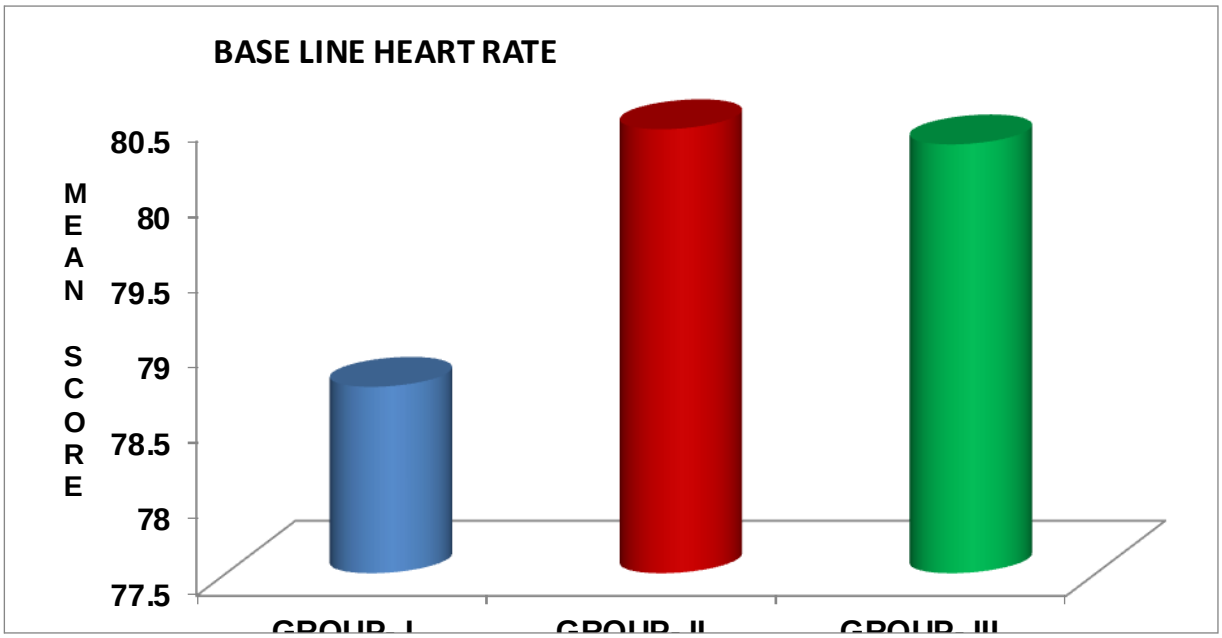
TABLE .4 Hart Rate

Group	Mean	Standard Deviation
GROUP-I		5.62
GROUP-II	78.73	5.72
GROUP- III	80.33	6.08
F-value	0.81	
p-value	0.45 - Not Significant	

TABLE-5

Systolic Blood Pressure

Group	Mean	Standard Deviation
GROUP-I	127.50	7.73
GROUP-II	127.50	8.47
GROUP- III	124.00	7.30
t-value	1.99	
p-value	0.14	
Significant	**Not Significant**	



SYSTOLIC BLOOD PRESSURE

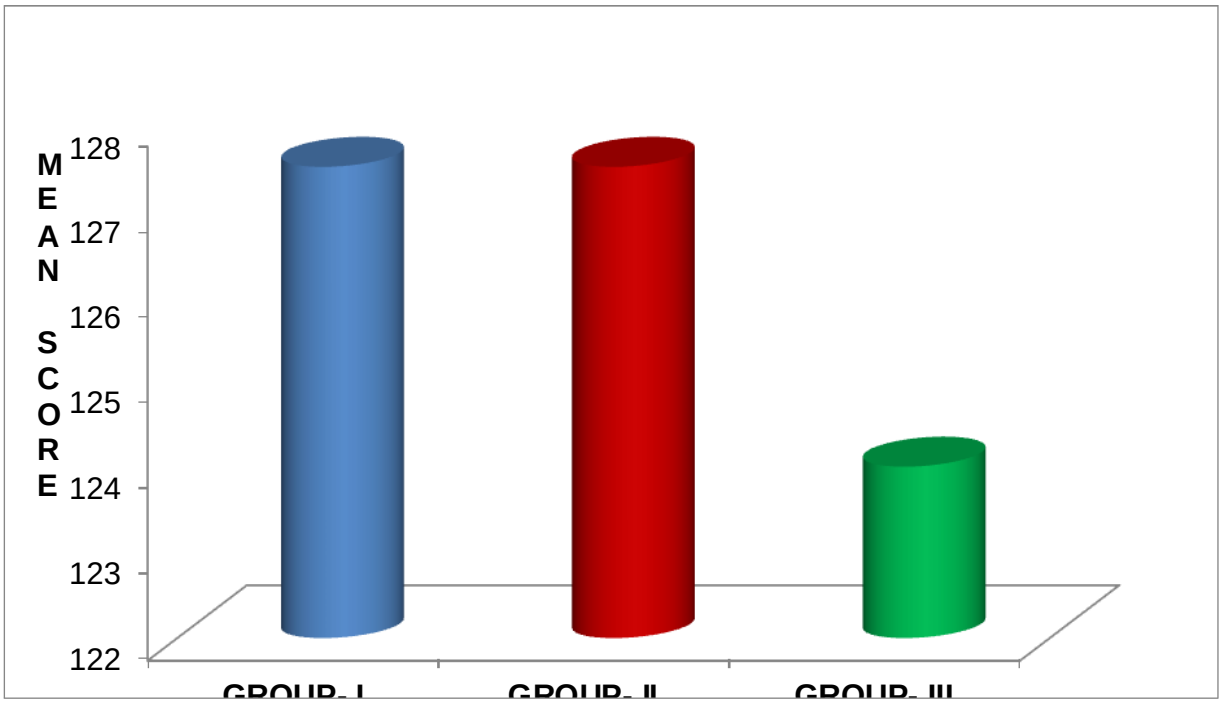


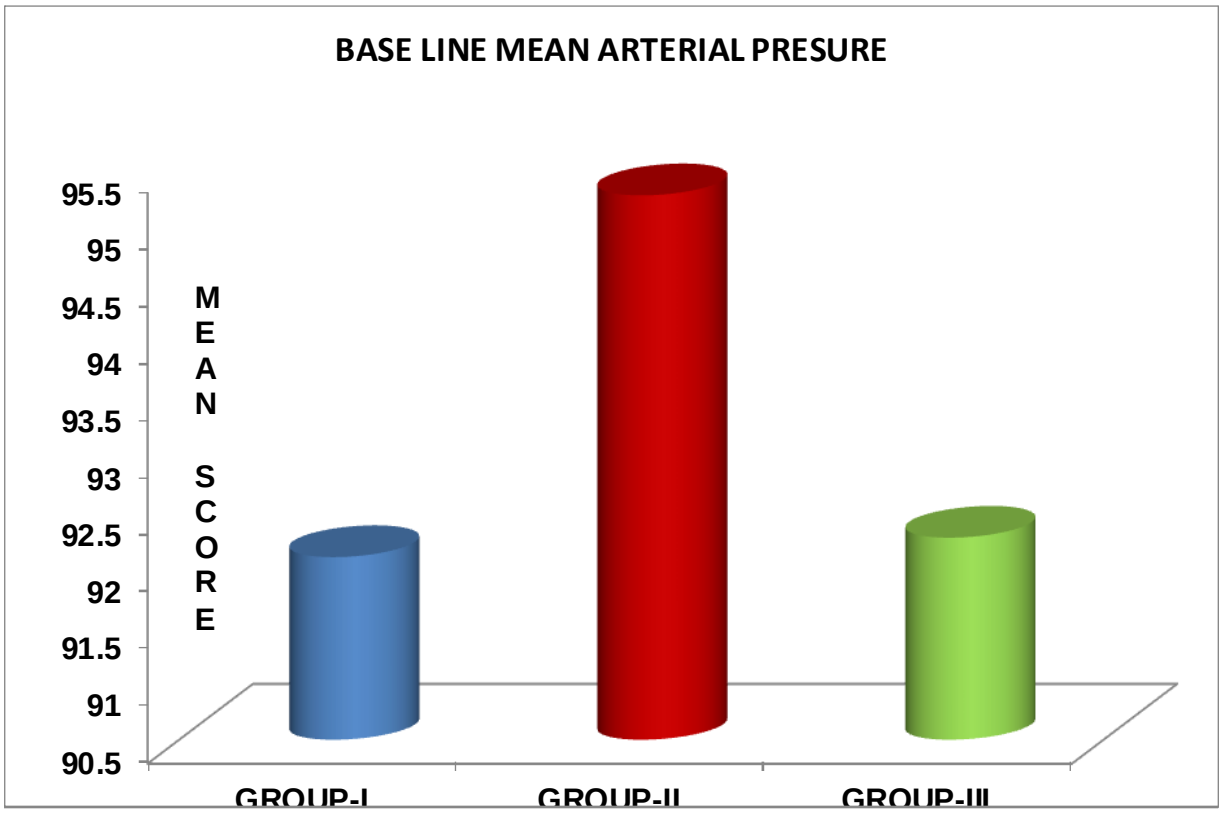
TABLE-6

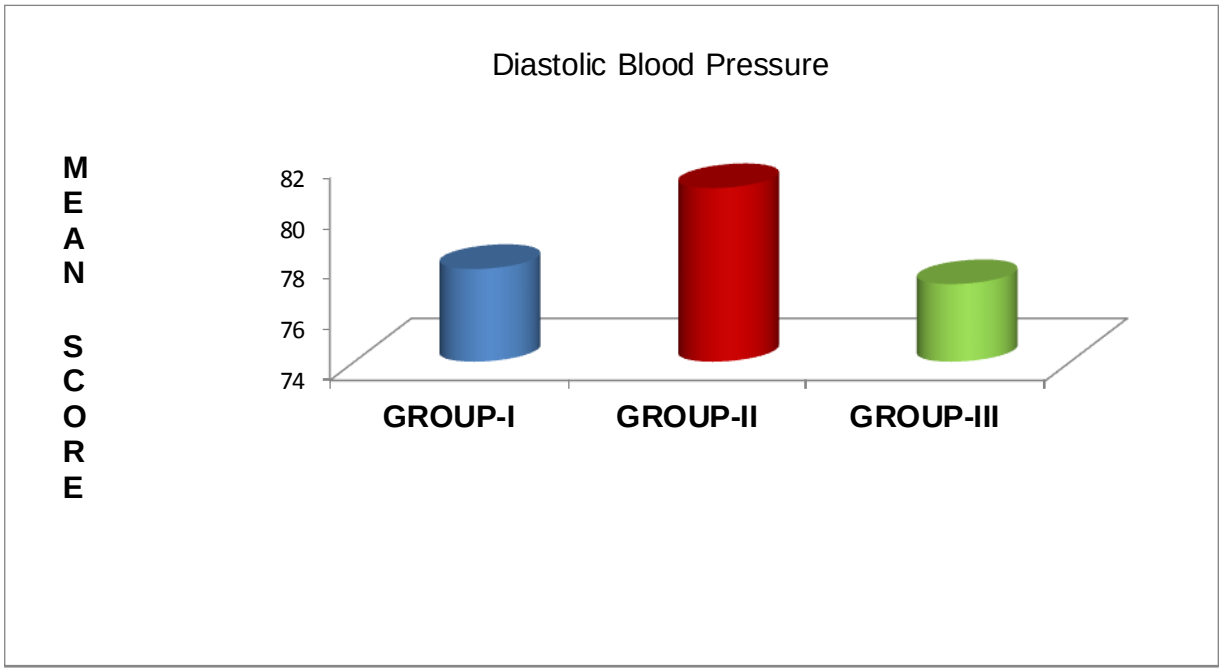
Diastolic Blood Pressure

Group	Mean	Standard Deviation
GROUP-I	77.67	5.76
GROUP-II	80.87	7.82
GROUP-III	77.07	6.39
F-Value	2.78	
p-value	0.07	
Significant	**Not Significant**	

TABLE-7. Mean Arterial Pressure

Group	Mean	Standard Deviation
GROUP-I	92.10	6.48
GROUP-II	95.27	8.57
GROUP-III	92.27	5.48
F-value	1.97	
p-value	0.15 - Not Significant	


BASE LINE MEAN ARTERIAL PRESURE
95.5
95
94.5
94
93.5
93
92.5
92
91.5
91
90.5
MEAN SCORE
GROUP-I
GROUP-II
GROUP-III


Diastolic Blood Pressure
MEAN SCORE
82
80
78
76
74
GROUP-I
GROUP-II
GROUP-III

BASE LINE TEMPERATURES

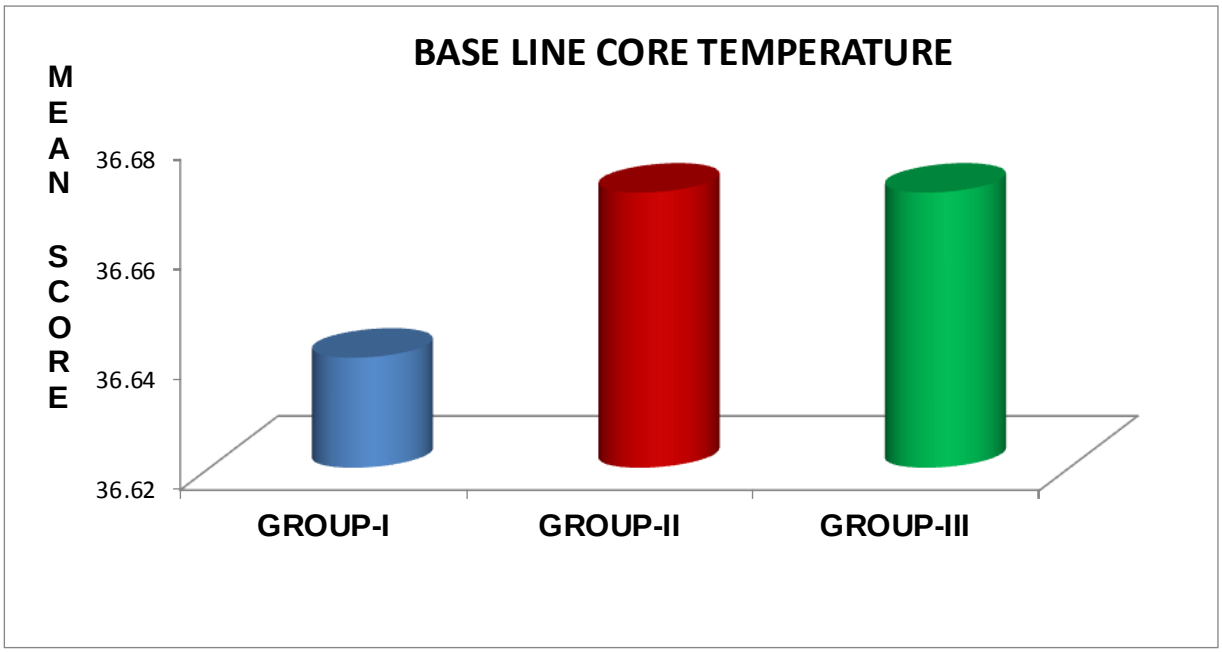
Base line temperatures of core, surface, and OT were recorded. Stastically the P-values were insignificant between three groups. These values were shown in the following tables.

TABLE-8 CORE TEMPERATURE

Group	Mean	Standard Deviation
GROUP-I	36.64	0.12
GROUP-II	36.67	0.12
GROUP-III	36.67	0.11
F-value	0.75	
p-value	0.48	
Significant	**Not Significant**	

TABLE-9 OT TEMPERATURE

Group	Mean	Standard Deviation
GROUP-I	22.41	0.16
GROUP-II	22.41	0.16
GROUP-III	22.38	0.15
F-value	0.39	
p-value	0.68	
Significant	**Not Significant**	


BASE LINE CORE TEMPERATURE
MEAN SCORE
36.68
36.66
36.64
36.62
GROUP-I
GROUP-II
GROUP-III

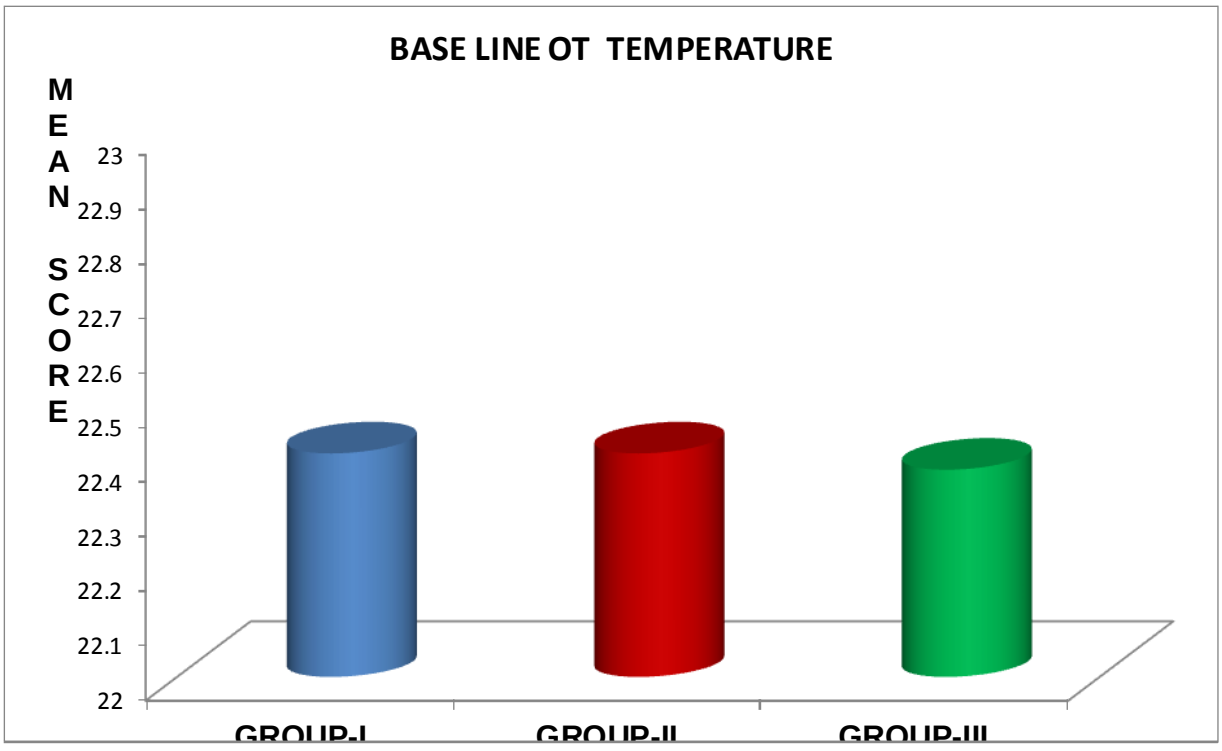
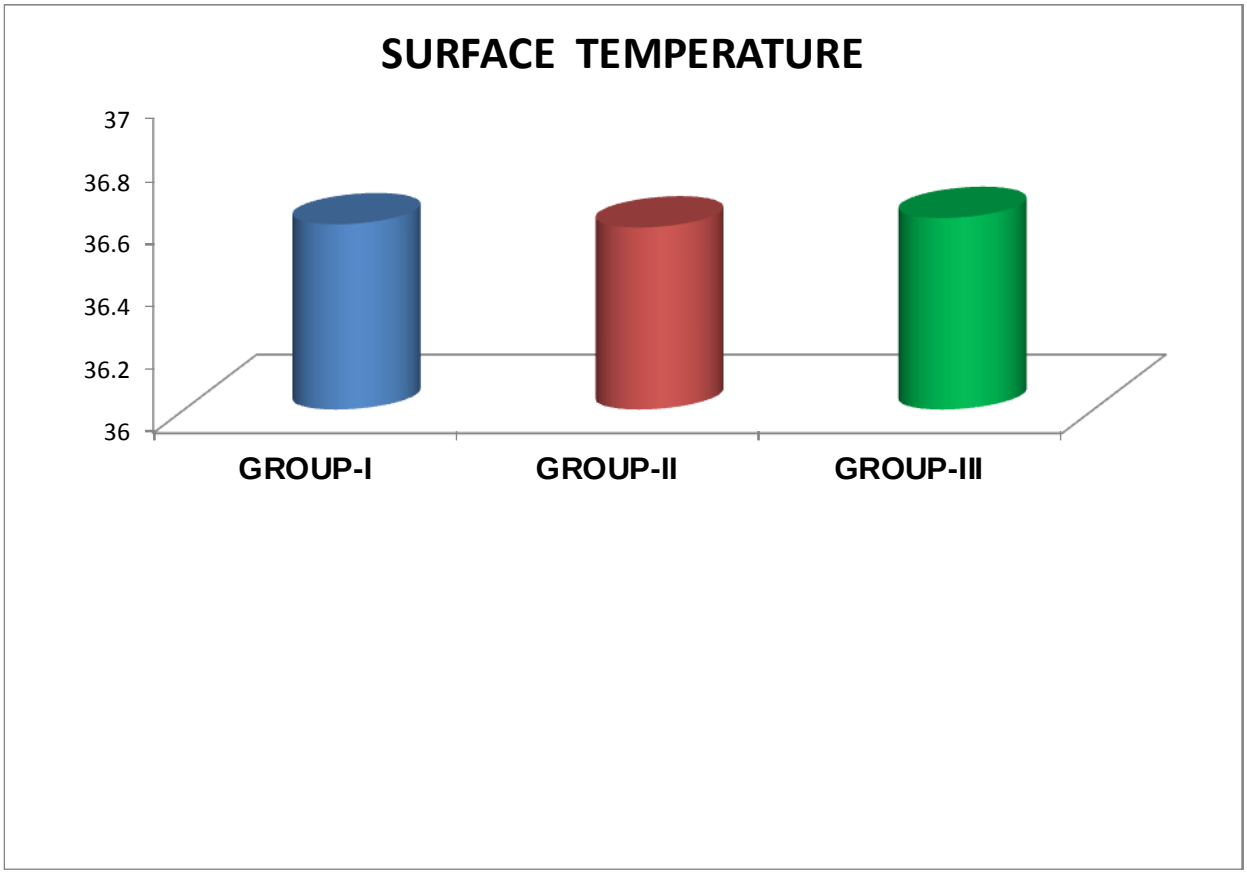
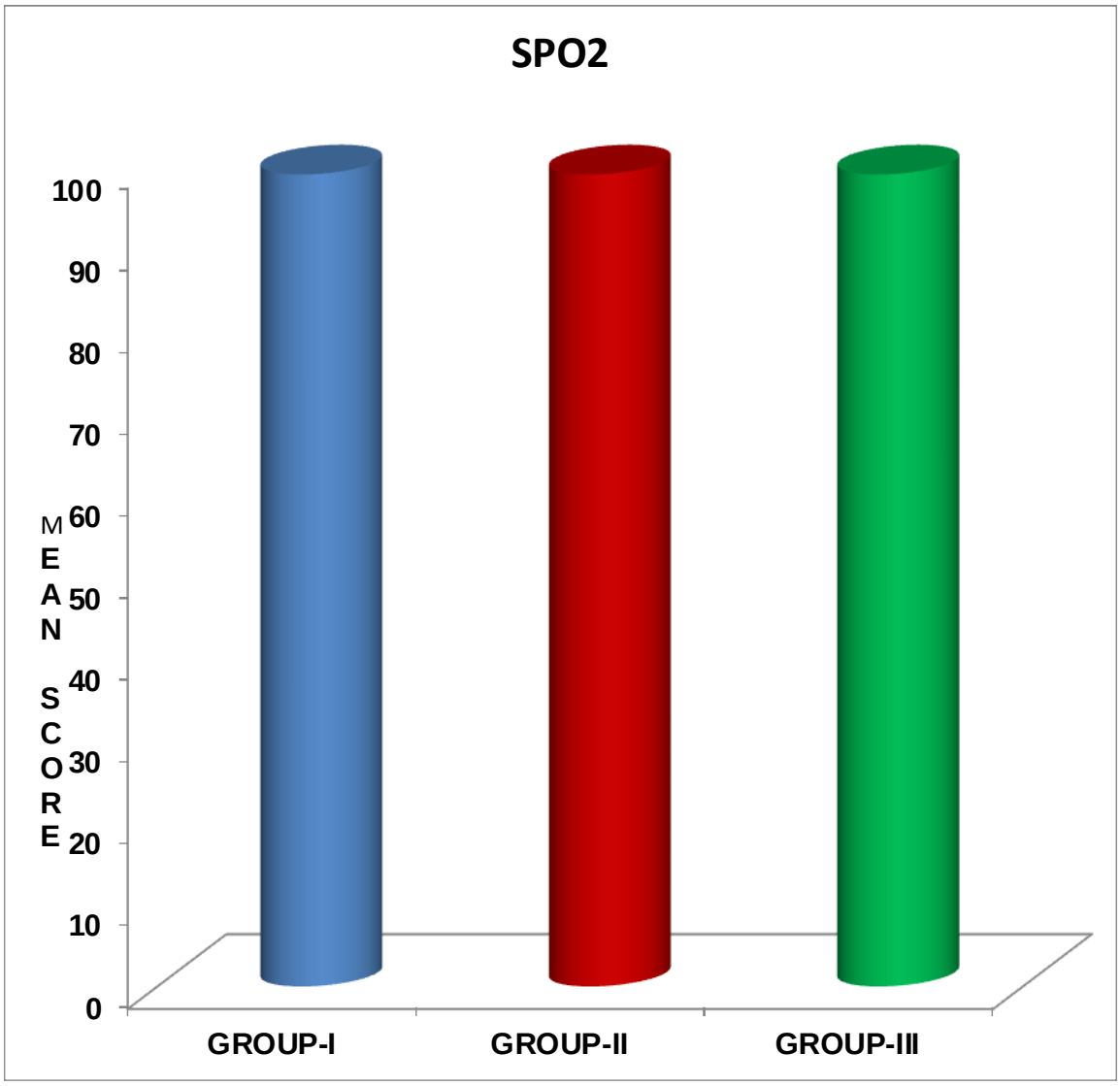

BASE LINE OT TEMPERATURE
MEAN SCORE
23
22.9
22.8
22.7
22.6
22.5
22.4
22.3
22.2
22.1
22
GROUP-I
GROUP-II
GROUP-III

TABLE-10 SURFACE TEMPERATURE

Group	Mean	Standard Deviation
GROUP-I	36.59	0.14
GROUP-II	36.58	0.13
GROUP-III	36.61	0.13
F-value	0.39	
p-value	0.68	
Significant	**Not Significant**	





The OT temperature P value 0.68, surface temperature value P-0.68 and core temperatures P value 0.48 insignificant were comparable between three groups.

TABLE-11INTRA OPERATIVE HEART RATE /min

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	79.50	5.84	82.13	5.88	80.57	4.49	**1.78**	**0.18**
30	80.63	6.20	80.20	5.52	78.83	3.89	**0.95**	**0.39**
45	81.57	4.77	79.13	5.08	81.53	4.65	**2.50**	**0.09**
60	82.07	4.86	82.13	5.88	82.47	4.47	**0.05**	**0.95**
75	81.97	5.63	79.90	4.35	81.27	6.14	**1.13**	**0.33**
90	81.57	4.77	79.97	4.52	80.43	5.46	**0.84**	**0.44**
105	80.73	4.65	80.13	4.81	79.67	5.13	**0.36**	**0.70**
120	79.43	4.52	80.13	4.81	80.50	4.87	**0.39**	**0.68**
135								
150								
165								
180								

*-**Significant**

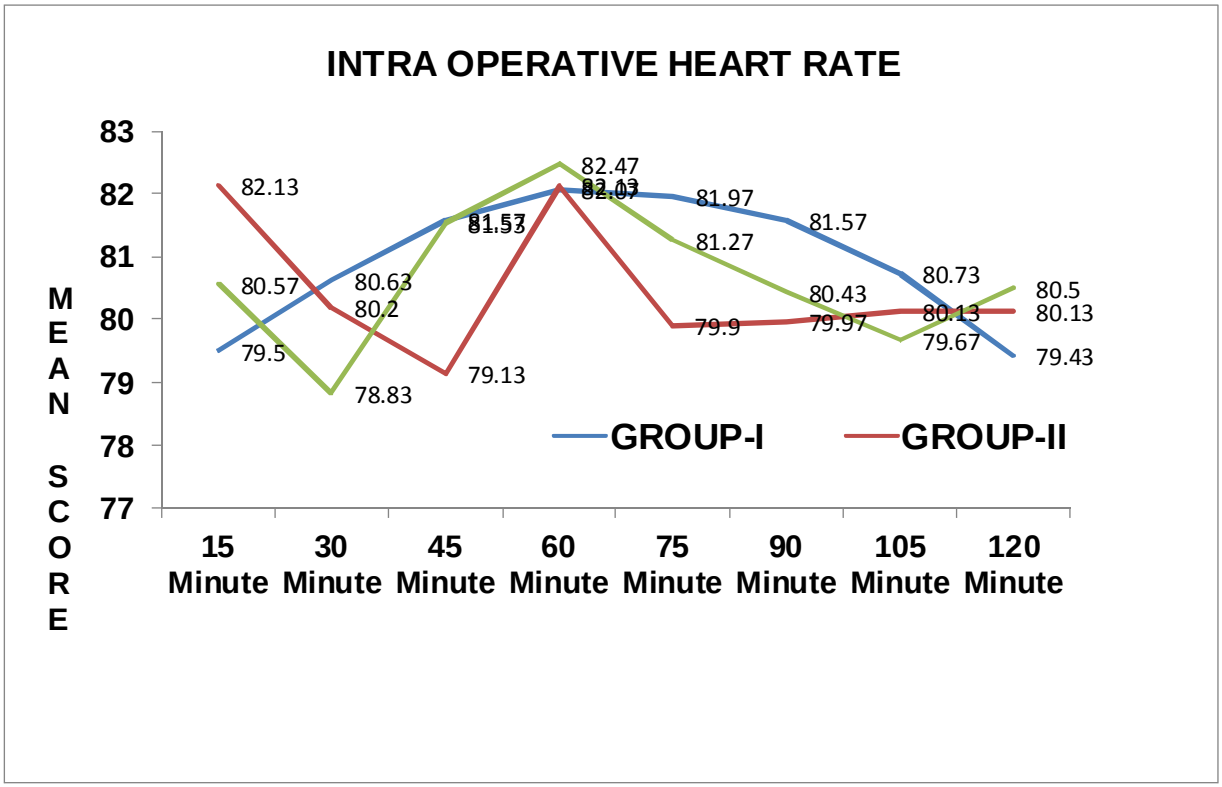
TABLE-12

INTRA OPERATIVE SYSTOLIC BLOOD PRESSURE IN mmHg

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	125.37	8.73	126.90	7.17	127.17	9.31	0.40	0.67
30	124.33	8.01	127.10	9.71	129.37	8.39	2.87	0.06
45	131.50	8.64	127.10	9.71	129.37	6.39	0.01	1.00
60	122.63	7.12	125.90	6.52	125.37	7.56	1.06	0.35
75	125.43	7.76	125.17	7.79	123.27	6.60	0.76	0.47
90	123.43	8.59	125.30	9.32	123.67	6.14	0.47	0.62
105	124.73	7.62	124.20	7.23	125.87	5.99	0.45	0.64
120	126.47	5.54	124.57	5.46	124.60	8.22	0.83	0.44
135								
150								
165								
180								

*-**Significant**

INTRAOPERATIVEVITALS



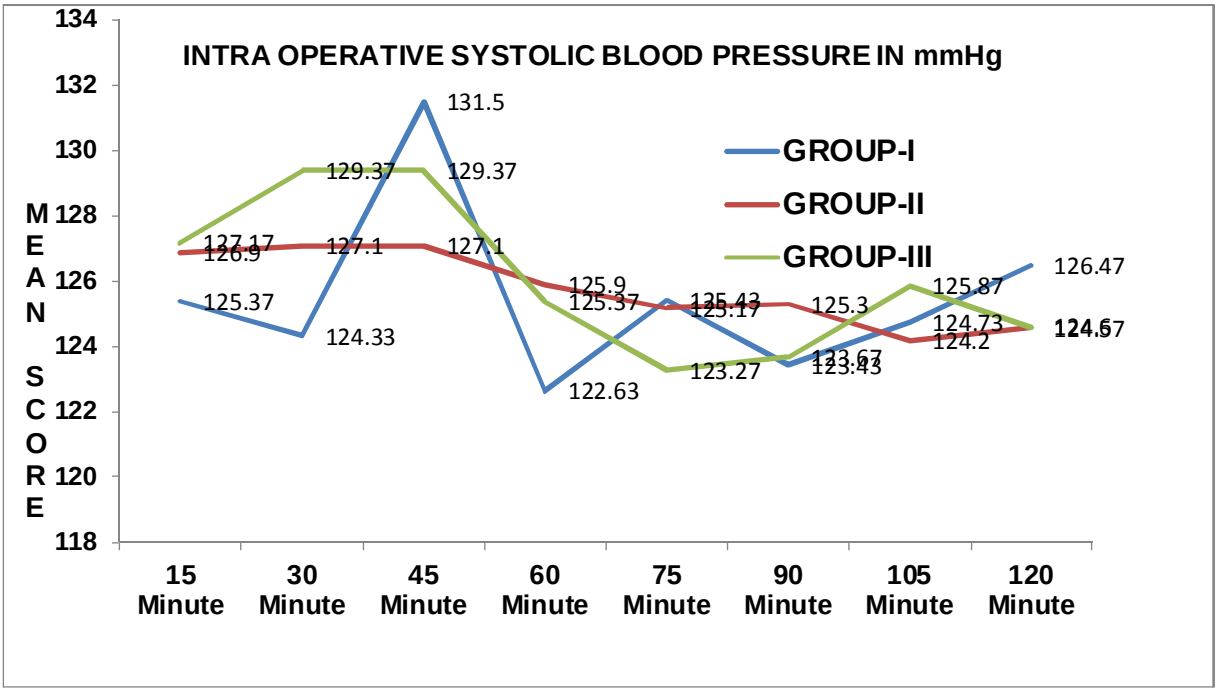


TABLE-13

INTRA OPERATIVE DIASTOLIC BLOOD PRESSURE IN mmHg

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	79.83	6.63	80.73	7.33	82.17	6.23	0.91	0.41
30	79.23	7.58	80.93	8.15	81.33	7.68	0.61	0.55
45	77.50	5.95	80.37	7.62	80.53	7.73	1.71	0.19
60	78.30	7.31	80.27	6.51	79.17	6.81	0.62	0.54
75	78.73	8.42	80.87	7.99	79.73	6.75	0.57	0.57
90	81.13	6.66	80.57	8.05	79.60	6.30	0.36	0.70
105	78.90	6.37	79.17	6.01	80.10	7.98	0.26	0.88
120	79.13	6.42	80.97	6.57	76.60	7.83	2.97	0.06
135								
150								
165								
180								

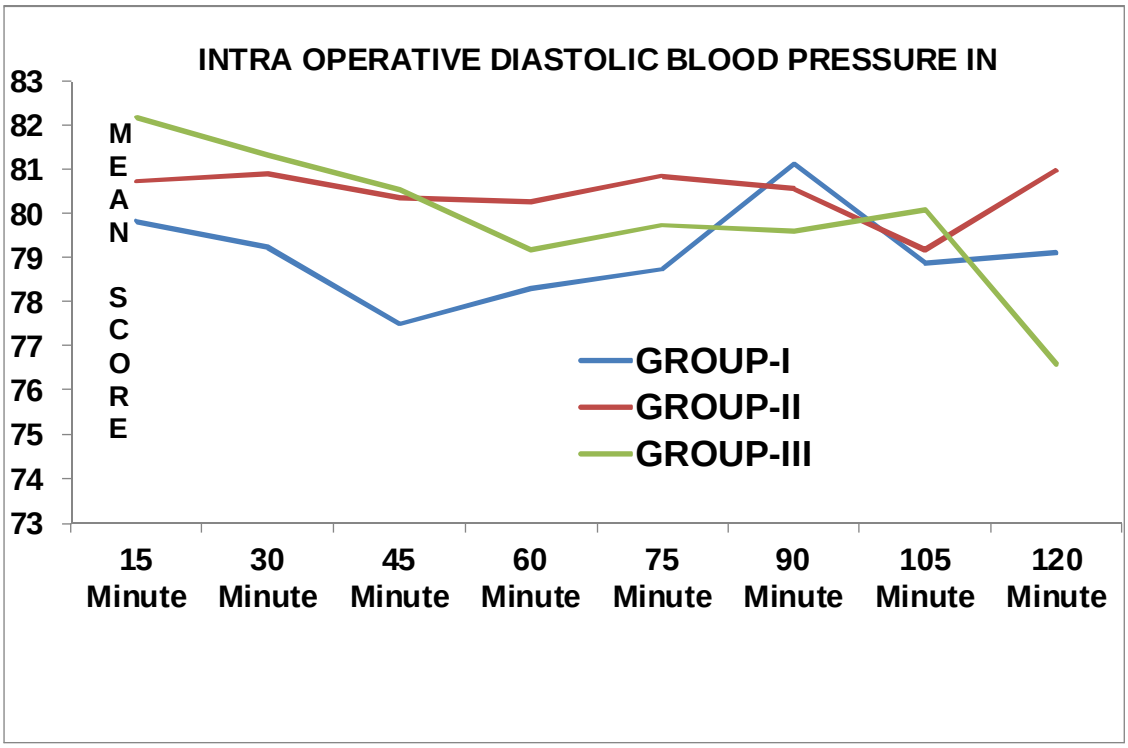
*-Significant

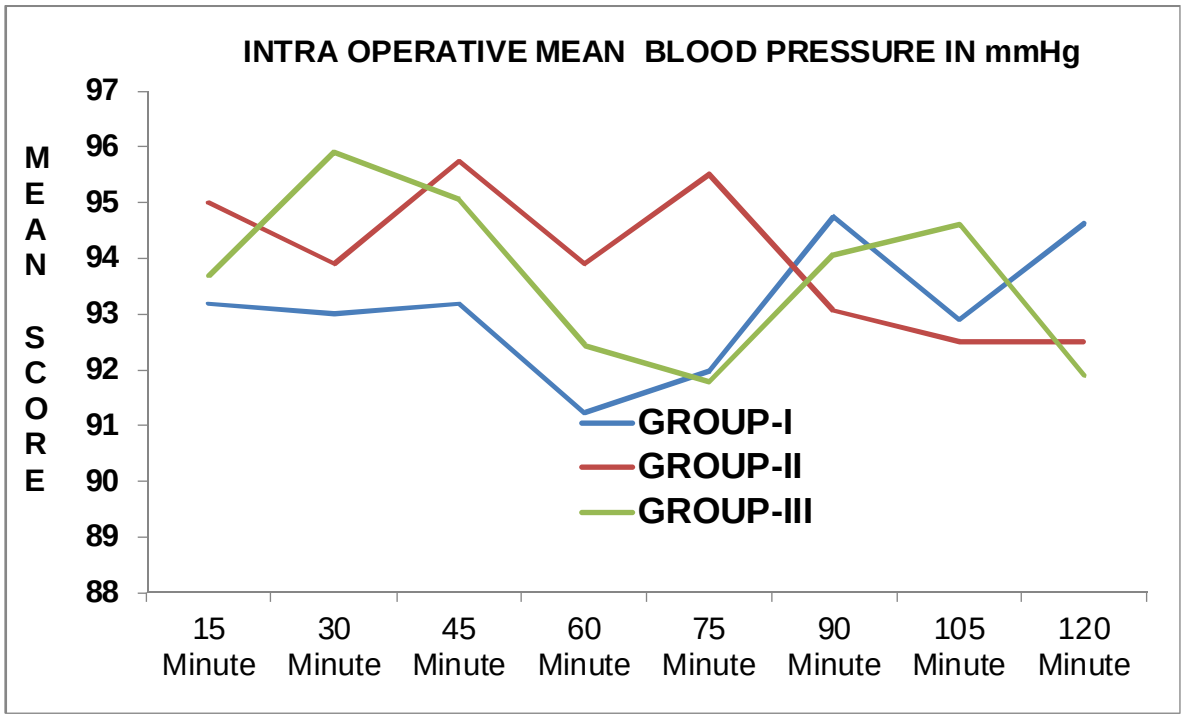
TABLE-14

INTRA OPERATIVE MEAN BLOOD PRESSURE IN mmHg

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	93.17	7.90	95.00	6.78	93.70	6.41	0.54	0.59
30	93.00	7.15	93.90	8.64	95.90	6.04	1.22	0.30
45	93.17	5.58	95.73	7.51	95.07	7.30	1.13	0.33
60	91.23	6.11	93.90	5.75	92.43	7.97	1.20	0.31
75	91.97	7.37	95.50	7.51	91.77	7.11	2.46	0.09
90	94.73	7.33	93.07	7.92	94.07	6.09	0.41	0.66
105	92.90	6.04	92.50	6.39	94.60	6.26	0.96	0.39
120	94.63	5.10	92.50	6.58	91.90	7.85	1.42	0.25
135								
150								
165								
180								

*-Significant


INTRA OPERATIVE DIASTOLIC BLOOD PRESSURE IN
MEAN SCORE
83
82
81
80
79
78
77
76
75
74
73
GROUP-I
GROUP-II
GROUP-III
15 Minute
30 Minute
45 Minute
60 Minute
75 Minute
90 Minute
105 Minute
120 Minute


INTRA OPERATIVE MEAN BLOOD PRESSURE IN mmHg
MEAN SCORE
97
96
95
94
93
92
91
90
89
88
GROUP-I
GROUP-II
GROUP-III
15 Minute
30 Minute
45 Minute
60 Minute
75 Minute
90 Minute
105 Minute
120 Minute

INTRAOPERATIVE TEMPERATURES

TABLE-15.

INTRA OPERATIVE SURFACE TEMPERATURE

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	36.60	0.14	36.58	0.13	36.59	0.11	0.22	0.81
30	36.51	0.10	36.49	0.10	36.48	0.10	0.10	0.91
45	36.22	0.30	36.16	0.33	36.10	0.36	0.003	1.00
60	36.08	0.26	36.15	0.23	36.14	0.23	0.09	0.92
75	36.05	0.22	36.06	0.20	36.02	0.34	0.01	1.00
90	36.02	0.24	36.06	0.16	36.11	0.17	0.08	0.92
105	35.95	0.31	35.94	0.19	35.93	0.23	0.01	1.00
120	35.89	0.22	35.92	0.19	35.92	0.18	0.002	1.00
135								
150								
165								
180								

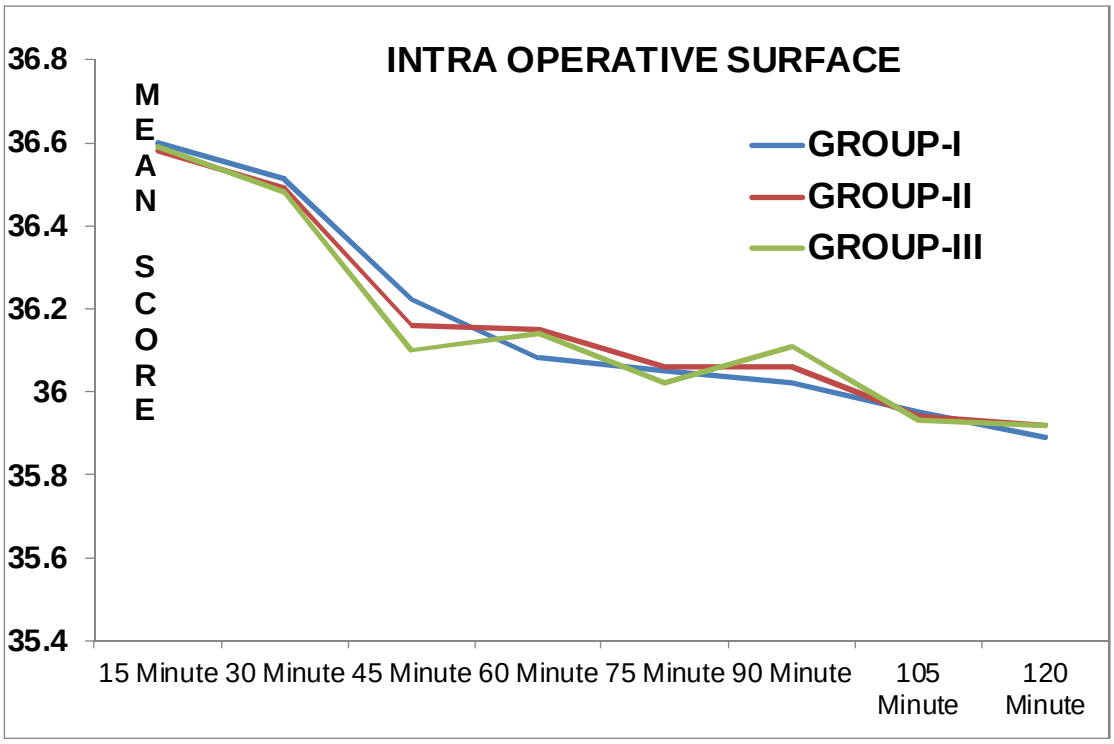
*-Significant

TABLE-16.

INTRA OPERATIVE OT TEMP

TIME	**GROUP-I**		**GROUP-II**		**GROUP-III**		**F-value**	**P-Value**
	Mean	**Sd**	**Mean**	**Sd**	**Mean**	**Sd**		
15	22.47	0.28	22.50	0.26	22.56	0.27	0.96	0.39
30	22.49	0.33	22.48	0.24	22.52	0.23	0.28	0.76
45	22.39	0.38	22.47	0.28	22.52	0.24	1.34	0.27
60	22.37	0.40	22.50	0.27	22.52	0.24	2.11	0.13
75	22.38	0.37	22.47	0.36	22.57	0.31	2.32	0.11
90	22.48	0.28	22.60	0.44	22.53	0.27	1.17	0.35
105	22.49	0.33	22.48	0.34	22.56	0.27	1.30	0.28
120	22.28	0.46	22.49	0.34	22.56	0.27	1.46	0.24
135								
150								
165								
180								

***-Significant**


INTRA OPERATIVE SURFACE
MEAN SCORE
36.8
36.6
36.4
36.2
36
35.8
35.6
35.4
GROUP-I
GROUP-II
GROUP-III
15 Minute
30 Minute
45 Minute
60 Minute
75 Minute
90 Minute
105 Minute
120 Minute

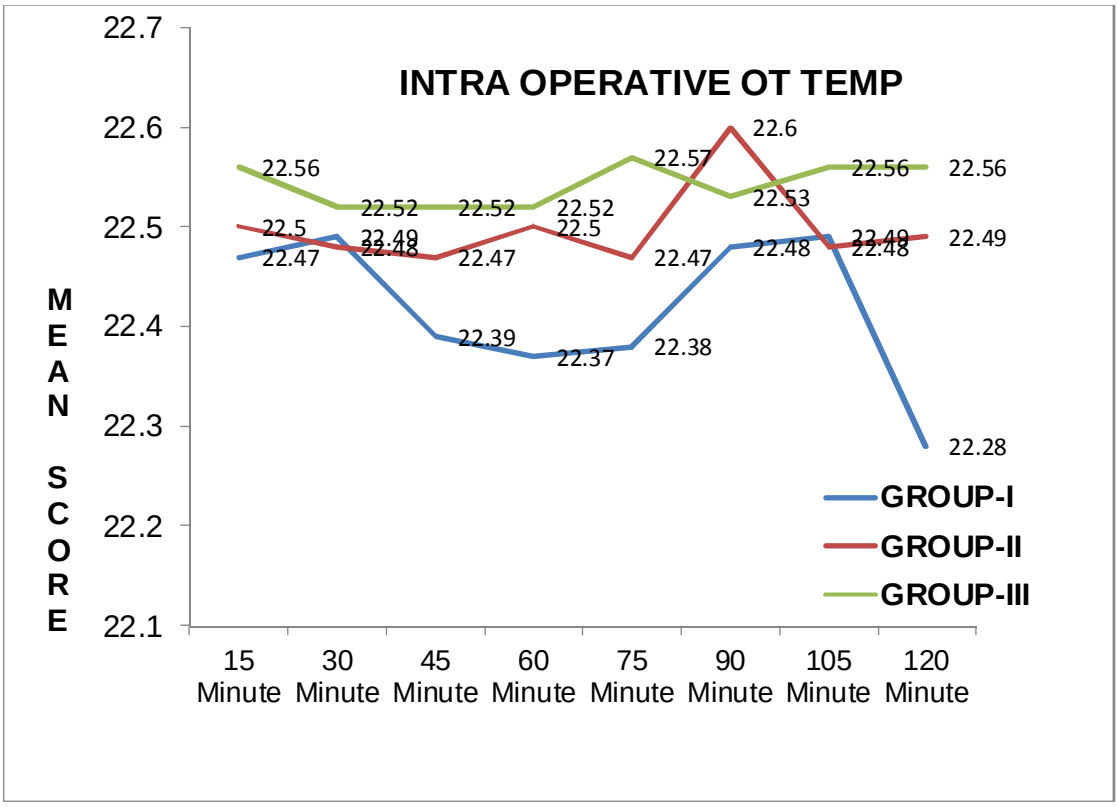

INTRA OPERATIVE OT TEMP
MEAN SCORE
22.7
22.6
22.5
22.4
22.3
22.2
22.1
22.56
22.52
22.52
22.52
22.57
22.53
22.56
22.56
22.5
22.49
22.48
22.47
22.5
22.47
22.48
22.49
22.48
22.6
22.47
22.39
22.37
22.38
22.28
GROUP-I
GROUP-II
GROUP-III
15 Minute
30 Minute
45 Minute
60 Minute
75 Minute
90 Minute
105 Minute
120 Minute

TABLE-17. INTRA OPERATIVE CORE TEMPERATURE

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	36.64	0.12	36.64	0.12	36.64	0.12	0.01	1.00
30	36.64	0.10	36.64	0.10	36.64	0.10	0.01	1.00
45	36.59	0.19	36.59	0.19	36.59	0.19	0.01	1.00
60	36.64	0.10	36.64	0.10	36.64	0.10	0.01	1.00
75	36.62	0.09	36.62	0.09	36.62	0.09	0.01	1.00
90	36.62	0.09	36.62	0.09	36.62	0.09	0.01	1.00
105	36.62	0.09	36.62	0.09	36.62	0.09	0.01	1.00
120	36.62	0.15	36.59	0.19	36.59	0.19	0.18	0.84
135								
150								
165								
180								

*-Significant

The P- values for intraoperative vitals Heart rate , SBP, DBP, MAP, Core temperature, surface temperature ,and OT temperatures were insignificant compared between three groups. They were shown in above tables.

After extubation post operative, Heart rate, SBP, DBP, MAP and SPO_2. Core temperature with nasopharyngeal probes, operation room temperature, and surface temperature with skin probes were monitored at 15, and 30 minutes. The P- values of post operative vitals and temperatures were insignificant, comparable between three groups. They were shown in following tables.

POST OPERATIVE VITALS

TABLE-18.

POST OPERATIVE HEART RATE/MIN

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	87.50	6.26	87.17	6.16	87.50	6.08	0.03	0.97
30	87.90	4.68	87.77	5.62	87.07	6.16	0.20	0.82

*-Significant

TABLE-19.

POST OPERATIVE SYSTOLIC BLOOD PRESSURE mmHg

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	126.53	3.44	126.83	5.94	126.20	3.21	0.16	0.86
30	128.37	5.06	127.70	4.07	127.50	4.54	0.30	0.75

*-Significant

TABLE-20. POST OPERATIVE DIASTOLIC BLOOD PRESSURE in mmHg

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	76.00	4.14	76.53	4.37	78.40	4.04	2.72	0.07
30	78.53	3.58	77.23	4.11	78.27	4.32	0.88	0.42

*-Significant

TABLE-21.

POST OPERATIVE MEAN ARTERIAL PRESSURE in mmHg

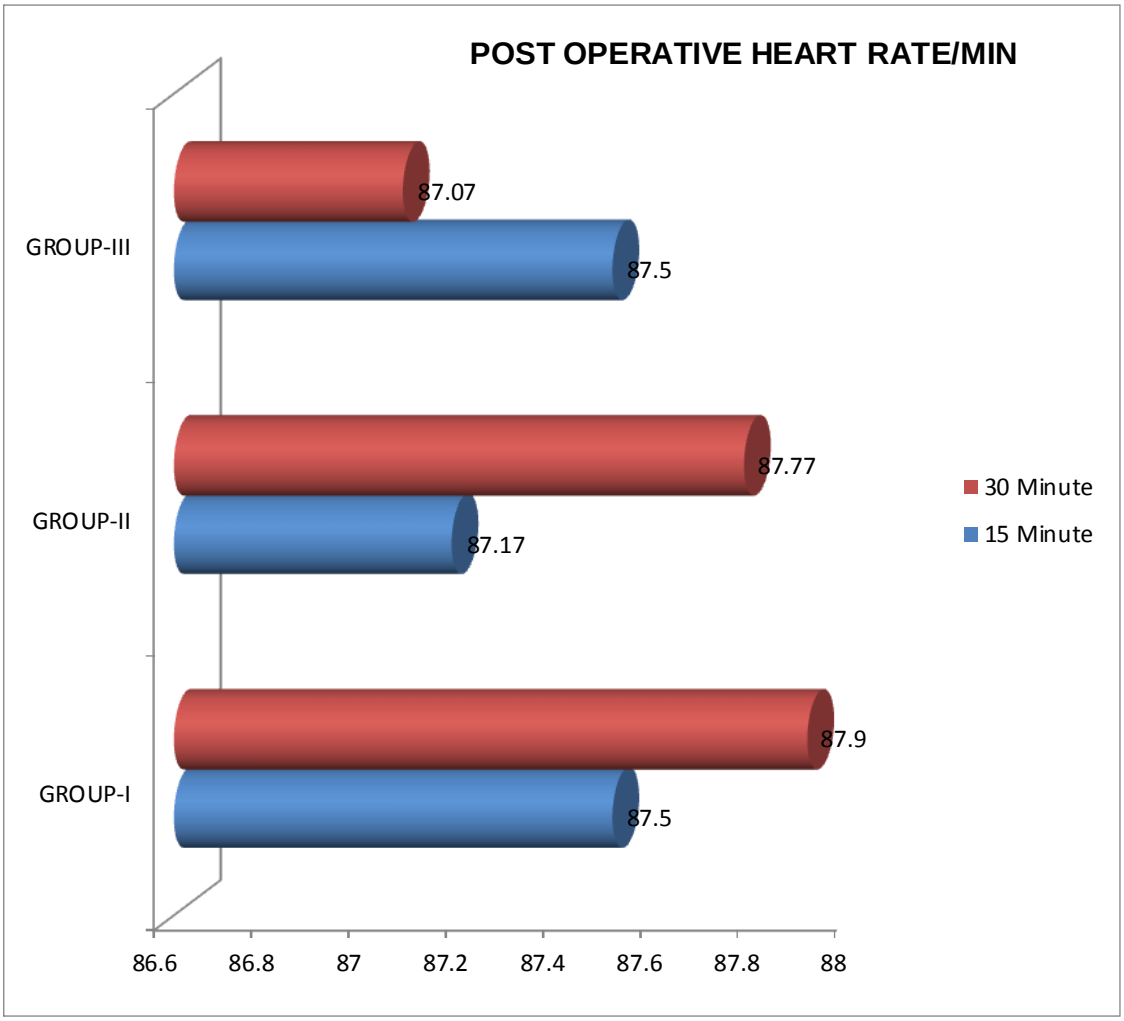
TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	92.67	3.62	93.10	4.33	92.67	3.81	0.12	0.89
30	94.37	3.74	93.60	3.87	94.17	3.96	0.32	0.73

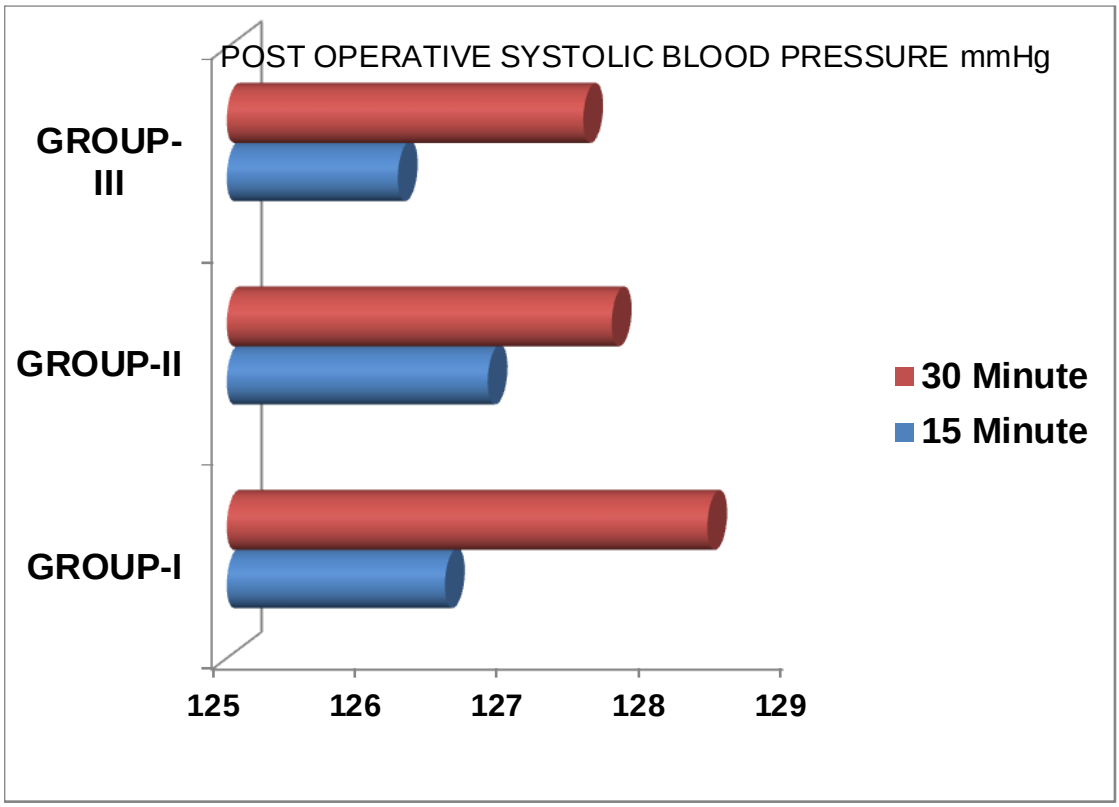
*-Significant

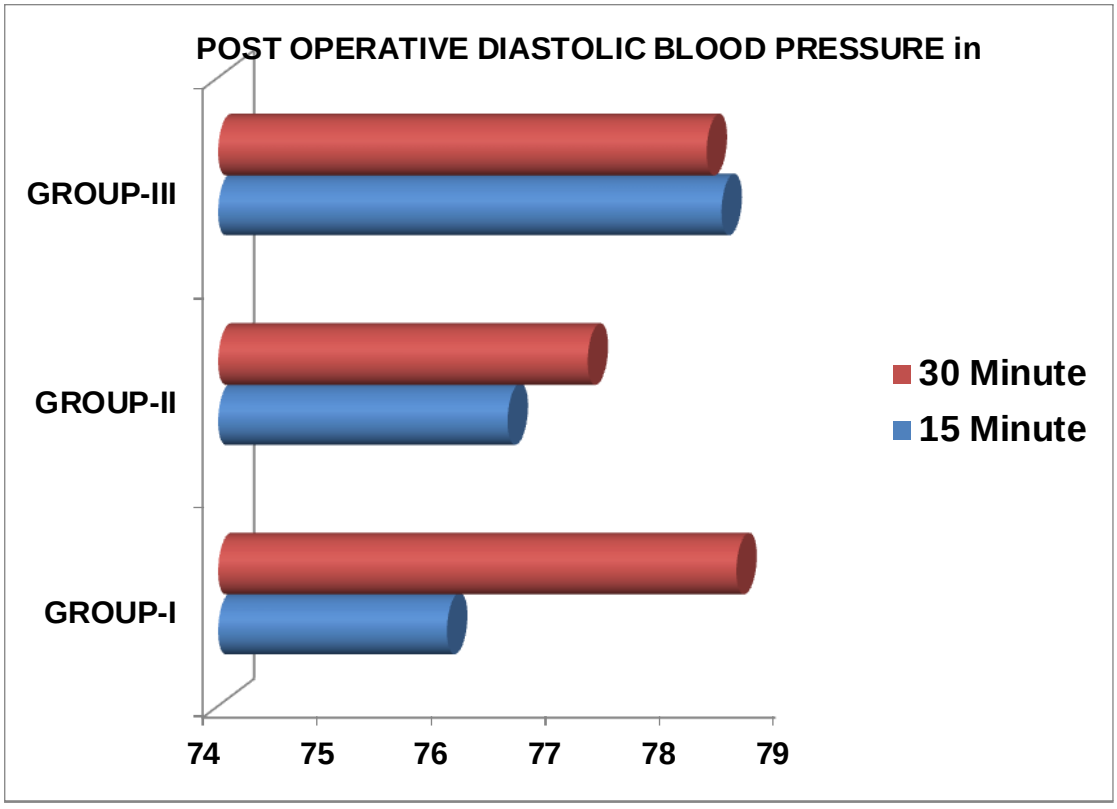
TABLE-22 POST OPERATIVE SPO2%

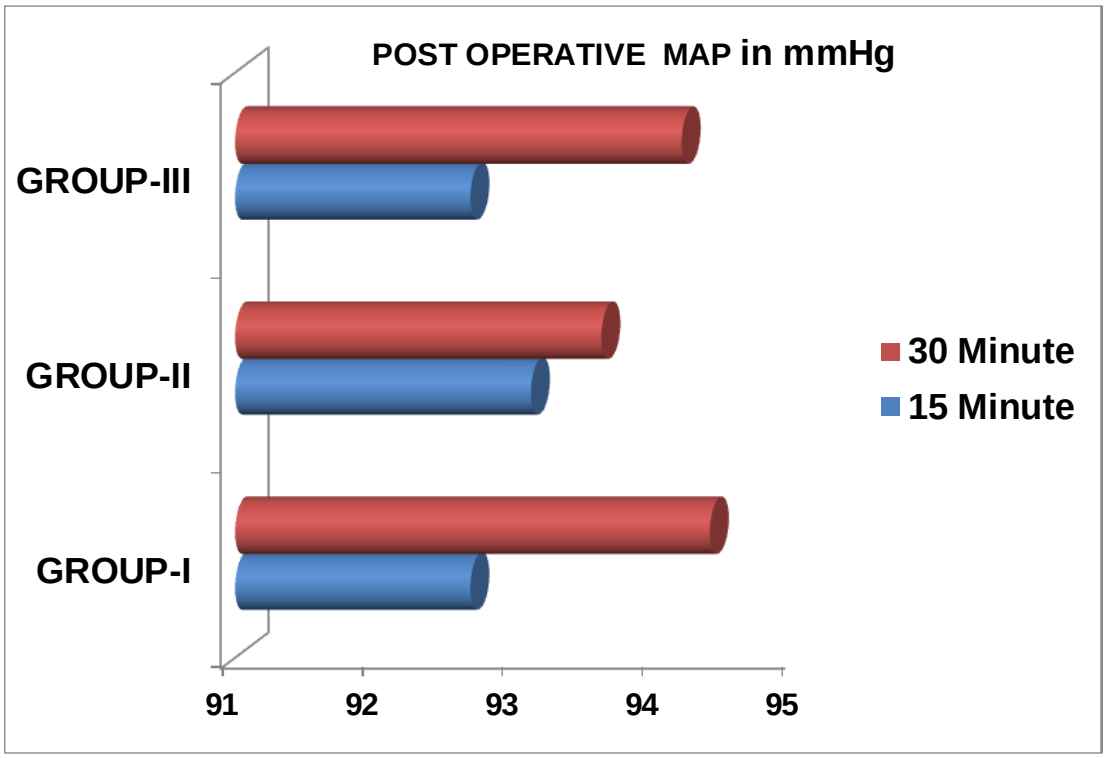
TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	99.00	0	99.00	0	99.00	0		
30	99.00	0	99.00	0	99.00	0		

*-Significant


POST OPERATIVE HEART RATE/MIN
GROUP-III
GROUP-II
GROUP-I
87.07
87.5
87.77
87.17
87.9
87.5
30 Minute
15 Minute
86.6
86.8
87
87.2
87.4
87.6
87.8
88


POST OPERATIVE SYSTOLIC BLOOD PRESSURE mmHg
GROUP-III
GROUP-II
GROUP-I
125
126
127
128
129
30 Minute
15 Minute


POST OPERATIVE DIASTOLIC BLOOD PRESSURE in
GROUP-III
GROUP-II
GROUP-I
74
75
76
77
78
79
30 Minute
15 Minute


POST OPERATIVE MAP in mmHg
GROUP-III
GROUP-II
GROUP-I
30 Minute
15 Minute
91
92
93
94
95

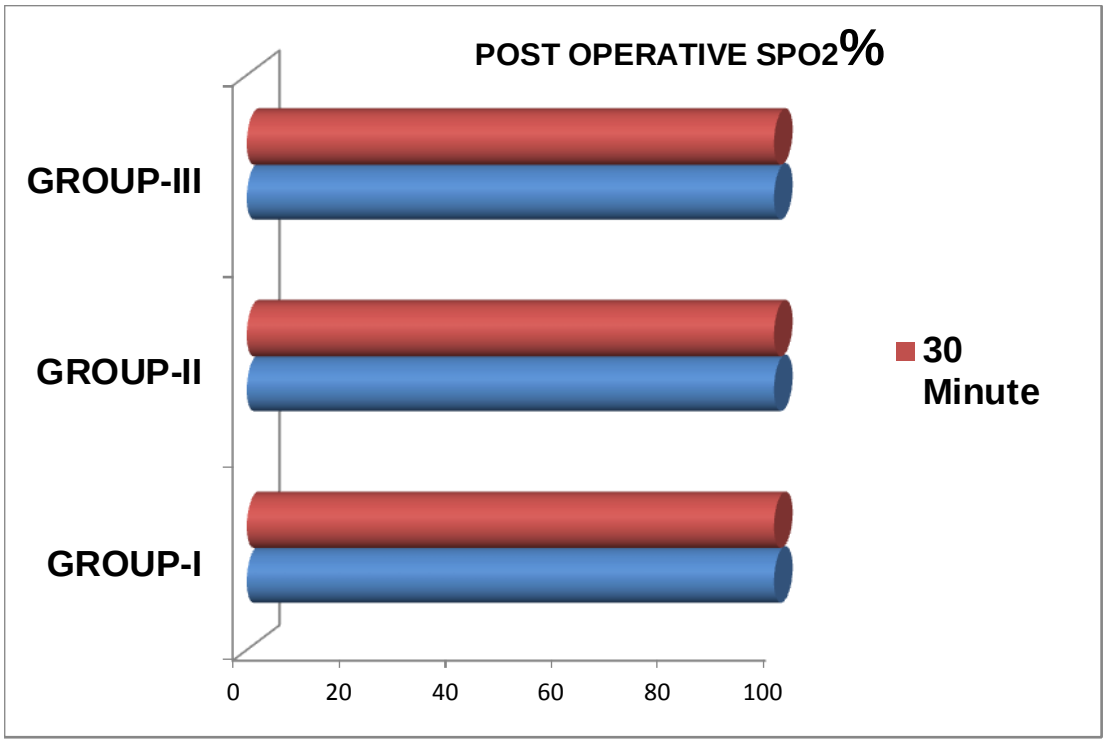

POST OPERATIVE SPO2%
GROUP-III
GROUP-II
GROUP-I
30 Minute
0
20
40
60
80
100

TABLE-25. POST OPERATIVE ROOM TEMP

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	22.39	0.38	22.37	0.40	22.38	0.37	0.04	0.96
30	22.48	0.28	22.44	0.35	22.49	0.33	0.20	0.82

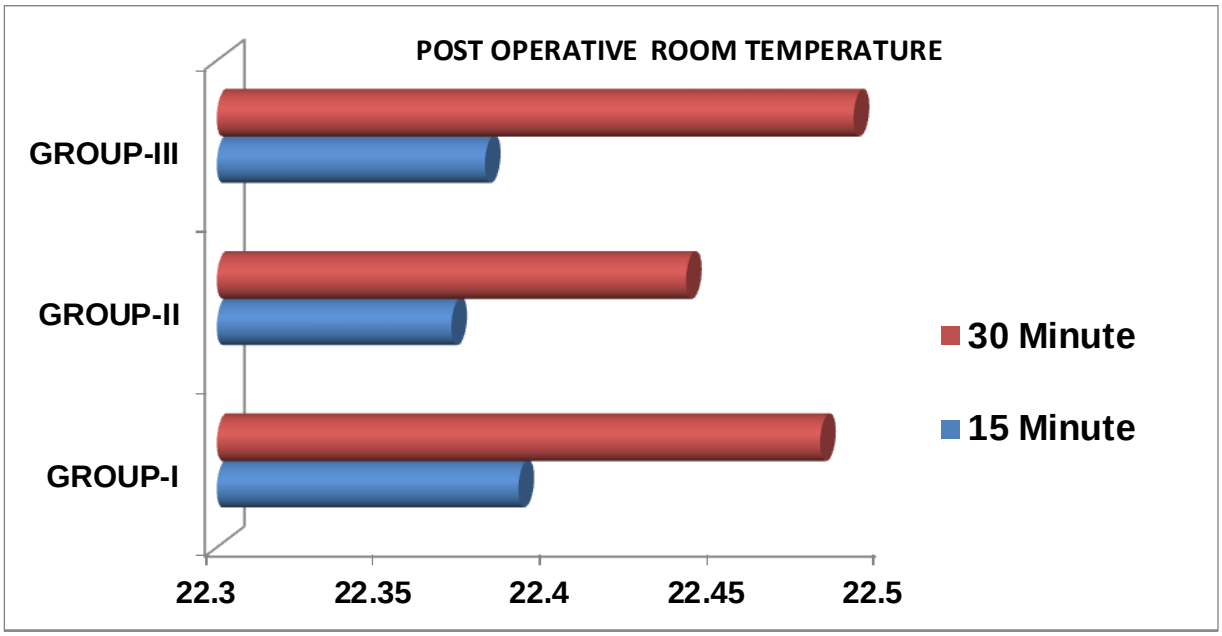
*-Significant

TABLE-26.

POST OPERATIVE CORE TEMPERATURE

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	36.64	0.10	36.61	0.15	36.64	0.10	0.65	0.53
30	36.64	0.10	36.64	0.10	36.59	0.19	1.21	0.30

*-Significant


POST OPERATIVE ROOM TEMPERATURE
GROUP-III
GROUP-II
GROUP-I
30 Minute
15 Minute
22.3
22.35
22.4
22.45
22.5

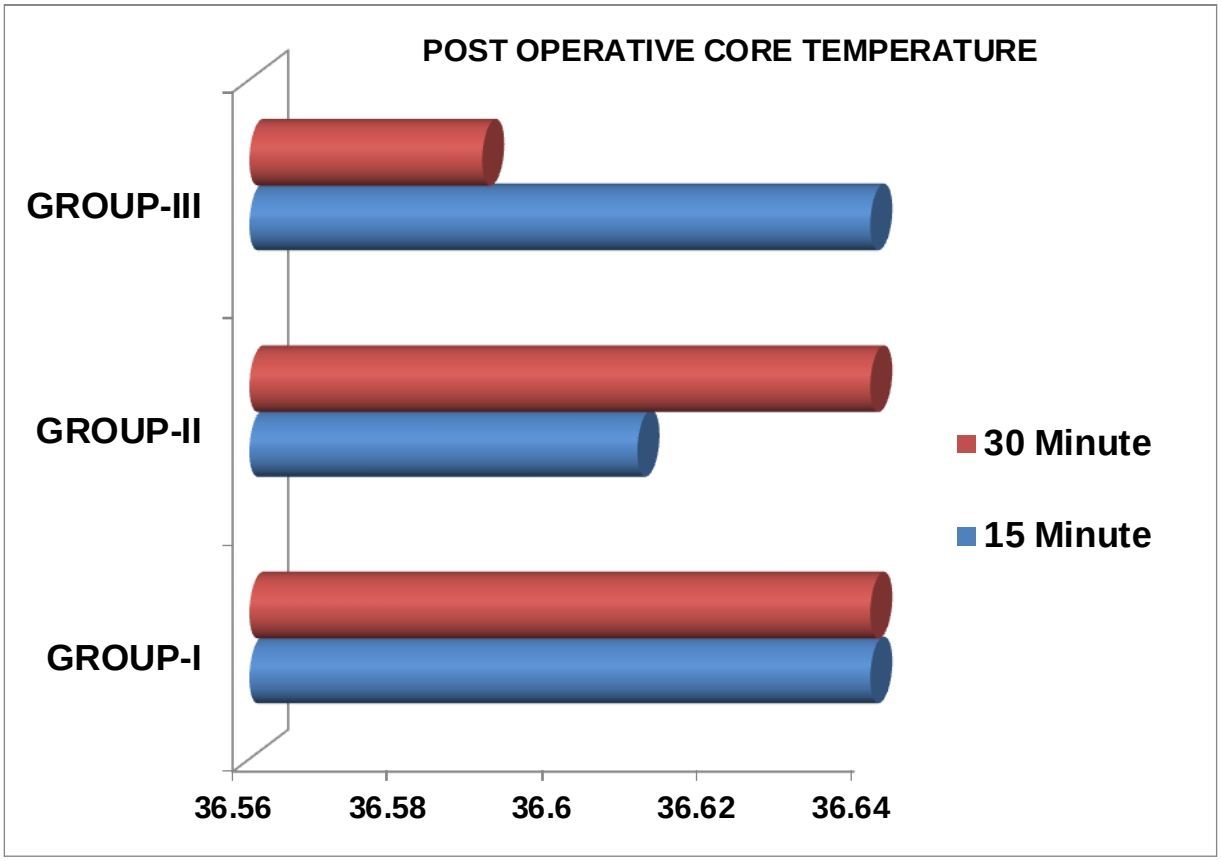

POST OPERATIVE CORE TEMPERATURE
GROUP-III
GROUP-II
GROUP-I
30 Minute
15 Minute
36.56
36.58
36.6
36.62
36.64

TABLE-27.POSTOPERATIVE SURFACE TEMPERATURE

TIME	GROUP-I		GROUP-II		GROUP-III		F-value	P-Value
	Mean	Sd	Mean	Sd	Mean	Sd		
15	36.62	0.09	36.62	0.15	36.68	0.39	0.62	0.54
30	36.62	0.09	36.58	0.13	36.62	0.09	1.52	0.23

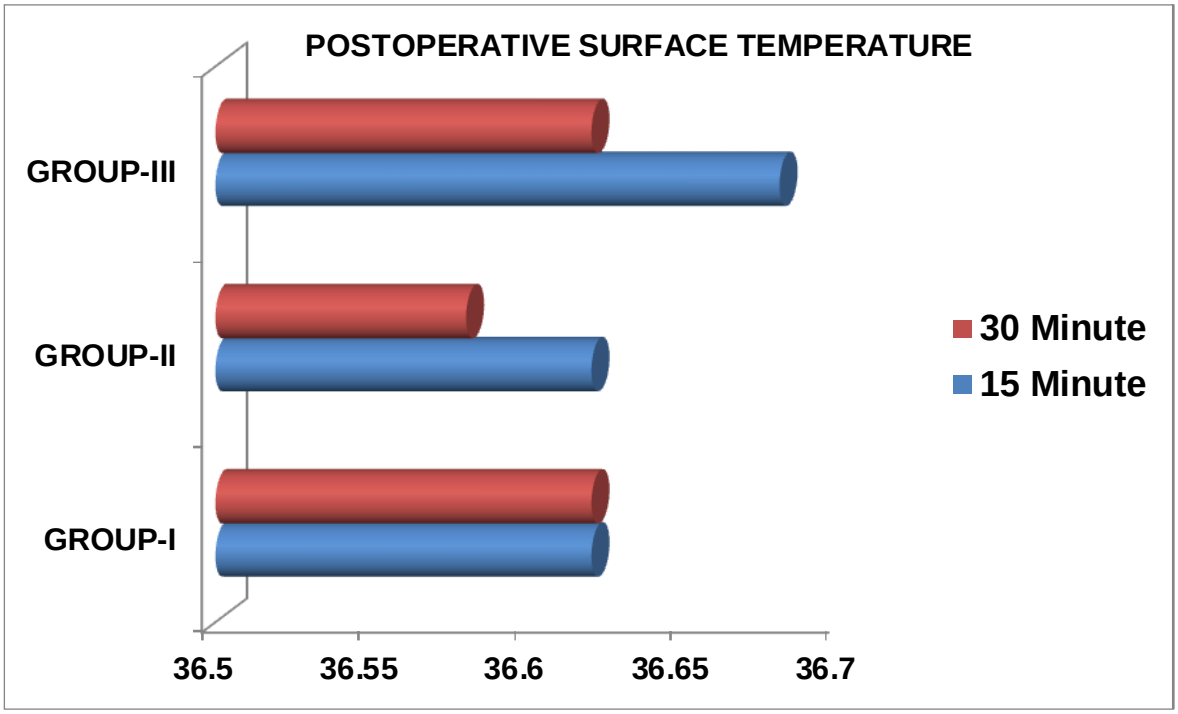


TABLE-28.

Variation in core Temperature score (Mean±sd) 30 Minutes

	Group-I	Group-II	Group-III	p-value	Significant
Pre-operative	36.64±0.12	36.67±0.12	36.67±0.11	0.48	NS
Post-operative(30min)	36.64±0.10	36.64±0.10	36.59±0.11	0.30	NS
Operative Difference	0.00±0.02	0.03±0.02	0.08±0.00	0.53	NS

** ANOVA Test

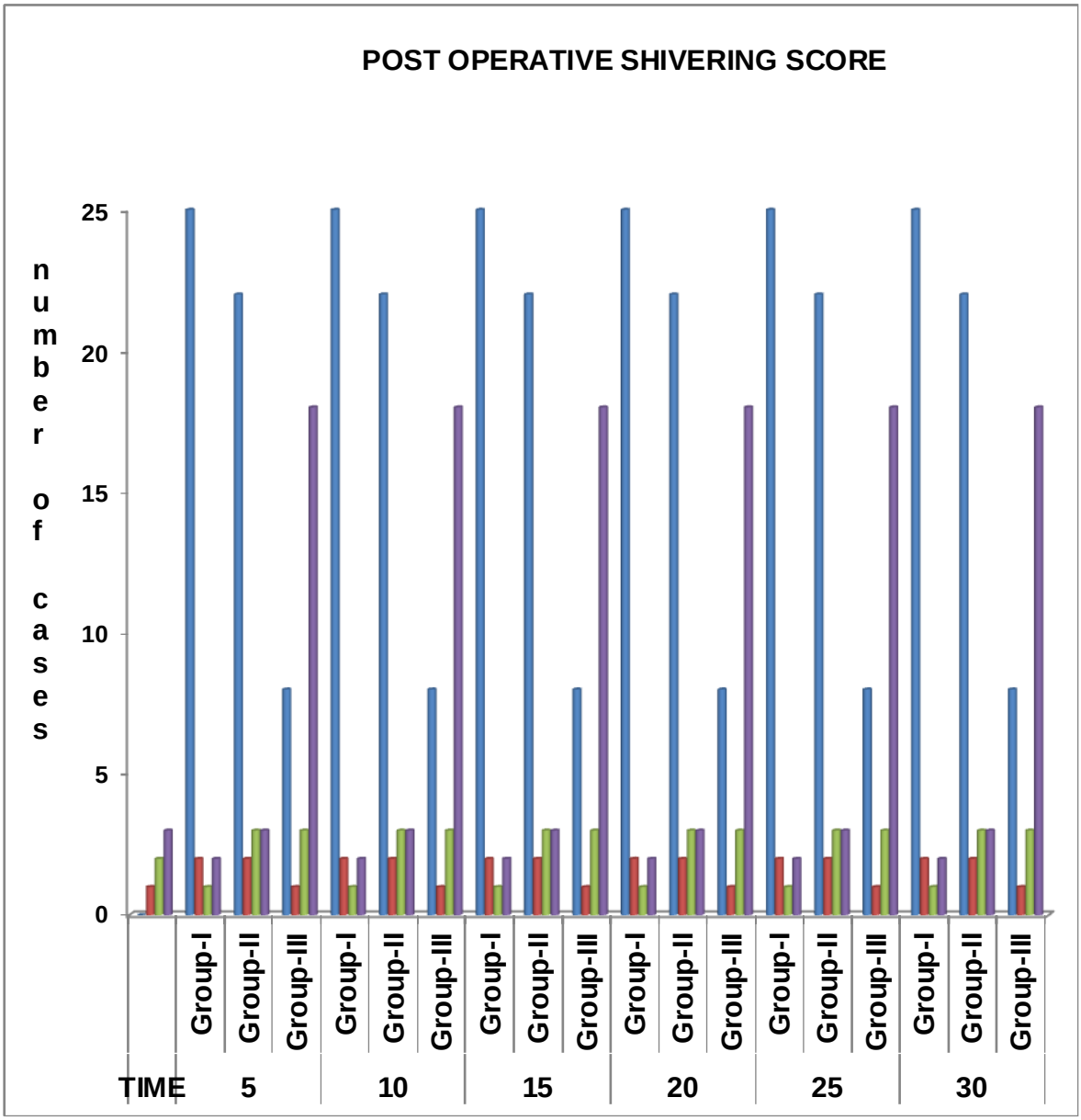
Iintraoperative and post operative temperature changes of P – value were not significant for three groups.

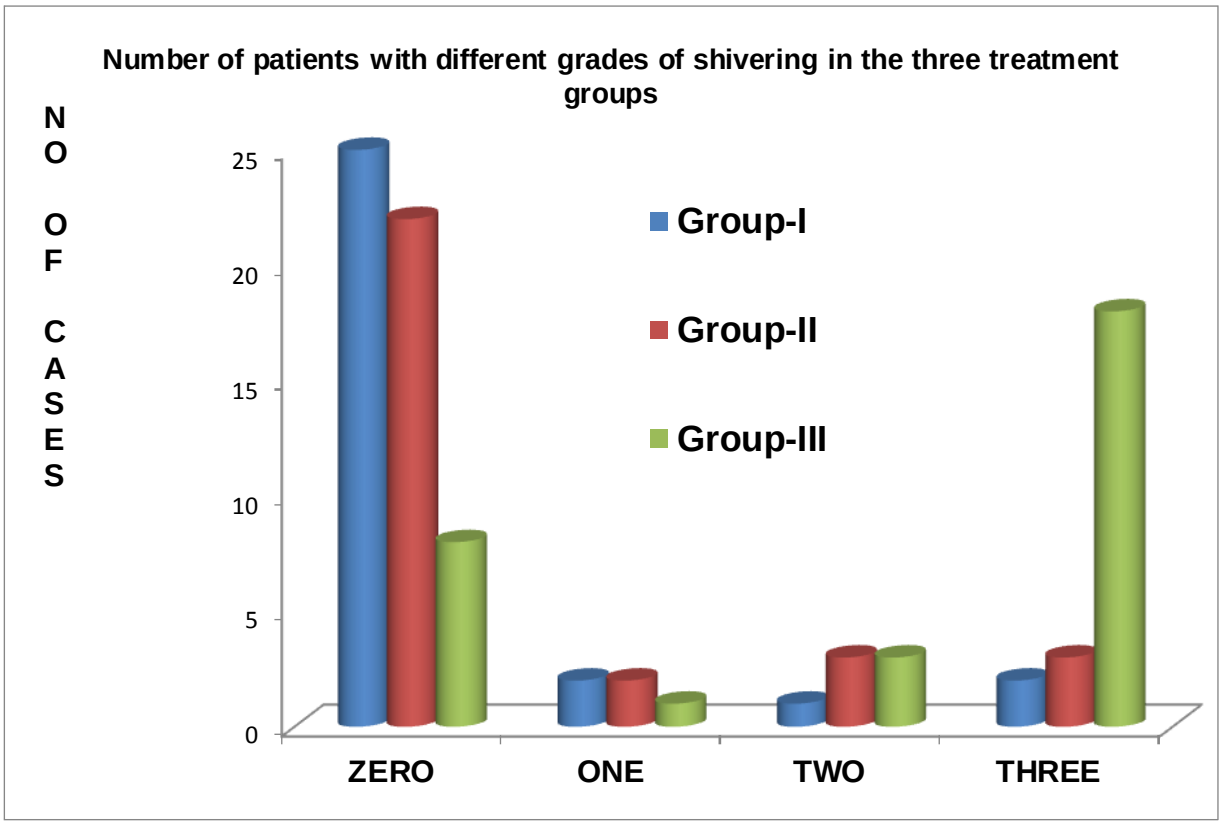
POST OPERATIVE SHIVERING SCORE

TABLE. 29.

TIME		0(%)	1(%)	2(%)	3(%)	Chi-Square	p-value	Significant
15	Group-I	25 (83.33)	2 (6.67)	1 (3.33)	2 (6.67)			
	Group-II	22 (73.33)	2 (6.67)	3 (10.00)	3 (10.00)	31.48	0.000	Significant
	Group-III	8 (26.67)	1 (3.33)	3 (10.00)	18 (60.00)			
30	Group-I	25 (83.33)	2 (6.67)	1 (3.33)	2 (6.67)			
	Group-II	22 (73.33)	2 (6.67)	3 (10.00)	3 (10.00)	31.48	0.000	Significant
	Group-III	8 (26.67)	1 (3.33)	3 (10.00)	18 (60.00)			

Post operative shivering graded after extubation at 15, and 30 minutes interval. No shivering occurs in Pethidine group 83.3% (n=25), Granisetron 73% (n=22), placebo group27% (n=8) P-value statistically not significant between Granisetron and Pethidine groups but significant ($P<0.05$) in placebo group. Shivering occurs at grade 3 in Pethidine group 7% (n=2), Granisetron10%(n=3), placebo group60%(n=18) P-value statistically not significant between Granisetron and Pethidine groups but significant in placebo group($P<0.05$).


POST OPERATIVE SHIVERING SCORE
number of cases
25
20
15
10
5
0
Group-I
Group-II
Group-III
TIME
5
10
15
20
25
30


Number of patients with different grades of shivering in the three treatment groups
NO OF CASES
25
20
15
10
5
0
Group-I
Group-II
Group-III
ZERO
ONE
TWO
THREE

DISCUSSION

The incidence of shivering in general anaesthesia is about 40% to 60 % [23] which depends upon the age, sex, drugs used and the duration of the surgery. The shivering can increase metabolic rate 600% above the basal value Postanaesthetic shivering is not only causing discomfort to the patients also increasing postoperative pain, also causes several physiological changes such as increased increased the tissue oxygen consumption and carbondioxide production and Lactic acidosis, mixed venous oxygen desaturation, and hypoxemia. which increase in minute ventilation , cardiac output and metabolic oxygen demand which results in increased stress on the patients with limited cardiopulmonary reserve and old age. Shivering is one of the low morbidity clinical outcomes among 33 causes was ranked as the sixth most important problem. During general anaesthesia onset of core hypothermia contributed by three factors which includes central thermoregulatory impairment, redistribution of heat from central to periphery, heat loss to the environment. The interthreshold range

increased for shivering and vasoconstriction .The cool ambient temperature environment in operation theater and cold intravenous fluids further decrease the temperature and cause shivering. In our study use of Granisetron 40µgm, and Pethidine25mg intravenously 5 minutes before induction of anaesthesia in patients undergoing general anaesthesia. Granisetron is 5HT receptor antagonist which used as an antiemetic clinically. Serotoninergic pathways play a significant role in the regulation of postoperative shivering. In our study no shivering occurs in Pethidine group 83.3%(n=25), Granisetron 73%(n=22), placebo group 27% (n=8) P-value statistically not significant between Granisetron and Pethidine groups but significant($P<0.05$) in placebo group. Shivering occurs at grade 3 in Pethidine group 7%(n=2), Granisetron 10% (n=3), placebo group 60% (n=18) P-value statistically not significant between Granisetron and Pethidine groups but significant in placebo group($P<0.05$). Similar results were derived by Asif Iqbal et al [(1)]. In Asif Iqbal and his colleagues study 2 patients in Pethidine group , 6 patients in Granisetron group had shivering they found that both drugs are equally effective for the prevention of postoperative

shivering. Powell and Buggy studied Ondansetron, a 5-HT3 antagonist and found that an intravenous dose of 8 mg a just prior to the induction of general anesthesia significantly reduced the incidence of postoperative shivering. This effect is probably due to a central inhibitory mechanism, given that there was no measurable effect on heat redistribution. These observations suggest that the serotoninergic pathways play a significant role in the regulation of postoperative shivering. Operation theater temperature no significant change in pre operative and postoperative in all three groups. Compare to placebo group shivering was significantly reduced in both Granisetron and Pethidine group. Beween study drug Granisetron and control group Pethidine equally effective.

SUMMARY

From this Prospective Randomized Double Blind Study we compared the Prophylactic Granisetron 40µgm per Kg body weight versus Pethidine 25mg, for the Prevention of Postoperative Shivering in patients undergoing Elective Thyroid Surgeries. During study and statistical analysis the following points were noted. The demographic profile like age, sex, weight, and height were compatible between three groups and statistically not significant. From our study we found that Granisetron and Pethidine were equally effective in preventing postoperative shivering when compared to placebo group

CONCLUSION

From this study the prophylactic use of both Granisetron and Pethidine were equally effective for the prevention of postoperative shivering.

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INSTITUTE ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI-3

EC Reg. No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 044 25363970

CERTIFICATE OF APPROVAL

To

Dr.C.Kalayarasi
Post Graduate M.D.(Anesthesiology),
Madras Medical College, Chennai -3.

Dear Dr. C.Kalayarasi

The Institutional Ethics Committee has considered your request and approved your study titled "A Prospective, Randomized Double Blind Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine, for the Prevention of Postoperative Shivering in Patients undergoing Elective Thyroid Surgeries" No.54082014.
The following members of Ethics Committee were present in the meeting held on 02.09.2014 conducted at Madras Medical College, Chennai -3.

1. Dr.C. Rajendran,MD	: Chairperson
2. Dr.V.Vimala,M.D. Dean,MMC,Chennai-3	: Deputy Chairperson
3. Prof.B.Kalaiselvi,M.D.,Vice-Principal,MMC,Ch-3	: Member Secretary
4. Prof.R.Nandhini,MD.Inst.of Pharmacology, MMC	: Member
5. Dr.G. Muralidharan,Director Incharge,Inst.of Surgery	: Member
6. Prof.K.Ramadevi,Director i/c.Inst.of Biochemistry, MMC	: Member
7. Prof.Saraswathy,MD.Director,Pathology, MMC	: Member
8. Prof.Tito,MD.Director,Pathology, MMC,	: Member
9. Thiru S.Rameshkumar, Administrative Officer	: Lay Person
10.Thiru S.Govindasamy,BA.BL.	: Lawyer
11.Tmt.Arnold Sauline,M.A.MSW	: Social Scientist

We approve the proposal to be conducted in its presented in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any6 changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

5/9/14

Member Secretary, Ethics Committee

2/9/14
MEMBER SECRETARY
INSTITUTIONAL ETHICS COMMITTEE
MADRAS MEDICAL COLLEGE

INTRODUCTION

Shivering after anaesthesia is the most frequent problem during the early recovery phase of general anaesthesia and also in neuroaxial anaesthesia. Incidence of postanaesthesia shivering occurs following general anaesthesia is between 40 – 60% .Postoperative shivering was in 6th position of among 33 [3] low morbidity clinical outcomes. The incidence of shivering following general anaesthesia or neuroaxial anaesthesia depends upon the room ambient temperature, genter, age

GROUP-3

S. No	NAME	AGE	SEX	WT kg	HT cms	HR/MIN	SBPmmHg	DBPmmHg	MAPmmHg	SPO2%	CORE TEMP	OT TEMP	SURFACE TEMP
	VASANTHA	42	F	60	152	88	122	82	95	99	36.7	22.6	36.5
2	KANAGAMMA	58	F	58	156	78	138	88	96	99	36.8	22.2	36.6
3	MANGMMAL	52	F	62	154	80	130	80	96	99	36.7	22.1	36.7
4	SEVANTHI	58	F	64	148	82	128	76	80	99	36.8	22.6	36.5
5	SANGEETHA	42	F	56	154	86	122	74	90	99	36.6	22.4	36.4
6	SUSHEELA	34	F	52	156	88	134	82	99	99	36.7	22.3	36.8
7	SUMATHI	38	F	58	158	90	110	70	83	99	36.8	22.5	36.6
8	SEETHA	39	F	49	157	84	126	70	88	99	36.5	22.4	36.5
9	SIVAGAMI	43	F	59	156	78	138	70	92	99	36.9	22.3	36.6
10	MANJULA	54	F	52	162	72	120	86	99	99	36.5	22.5	36.6
11	MALAR	43	F	58	152	76	120	72	88	99	36.7	22.2	36.5
12	MEENATCHI	48	F	48	154	78	114	72	86	99	36.7	22.4	36.8
13	CHINNAPONNU	56	F	51	156	68	118	78	99	99	36.8	22.5	36.6
14	KALAIVANI	32	F	61	158	76	122	80	94	99	36.7	22.2	36.7
15	TAMILSELVI	26	F	56	164	74	126	80	95	99	36.7	22.4	36.5
16	RADHAA	38	F	47	162	82	132	62	95	99	36.5	22.1	36.5
17	SULOCHANA	42	F	52	158	86	128	78	94	99	36.6	22.5	36.8
18	VELATH	59	F	58	156	77	114	74	86	99	36.6	22.4	36.7
19	SUMATHI	44	F	54	152	72	118	69	85	99	36.8	22.3	36.6
20	MADHU	46	F	56	154	78	115	71	85	99	36.7	22.2	36.6
21	MALARVIZHI	36	F	64	150	82	124	85	95	99	36.5	22.6	36.8
22	UMA	32	F	66	158	92	123	84	95	99	36.6	22.5	36.7
23	YESOTHA	46	F	62	152	84	136	80	95	99	36.7	22.3	36.8
24	SARANYA	32	F	67	154	72	123	81	100	99	36.7	22.4	36.5
25	VASANTHA	55	F	62	152	76	123	88	99	99	36.8	22.6	36.7
26	PAPA	58	F	56	156	78	115	82	98	99	36.5	22.3	36.4
27	ALAMELU	54	F	54	154	82	120	73	86	99	36.7	22.4	36.6
28	RANI	56	F	52	152	89	127	70	90	99	36.6	22.4	36.5
29	SOLAI	49	F	58	158	86	132	75	95	99	36.5	22.2	36.7
30	KALA	52	F	48	152	76	122	80	90	99	36.7	22.5	36.4

INTRA 0PERATIVE HEART RATE/MIN												INTRA OPERATIVE SYSTOLIC BLOOD PRESSURE IN mmHg												INTRAOPERATIVE DIASTOLIC BLOOD PRESSURE IN mmHg											
15	30	45	60	75	90	105	120	135	150	165	180	15	30	45	60	75	90	105	120	135	150	165	180	15	30	45	60	75	90	105	120	135	150	165	180
83	74	68	94	76	74	72	74					118	124	122	122	128	118	116	120					78	74	70	88	70	76	70	74				
75	77	86	82	81	82	75	72					125	116	114	120	116	109	130	117					91	88	78	76	71	69	81	73				
79	76	85	88	95	92	72	71					137	130	142	138	124	118	128	118					86	86	91	74	70	72	81	76				
79	80	82	86	78	74	86	78					130	143	143	129	130	124	132	135					86	85	84	70	81	82	76	90				
74	78	84	86	88	90	87	86					143	136	136	125	120	132	136	128					84	84	92	81	70	72	92	70				
78	84	82	87	83	86	82	84					134	118	128	1130	136	130	118	128					88	73	73	86	92	85	69	77				
84	78	86	82	84	79	84	78					132	132	156	132	112	134	134	118					79	82	98	82	76	88	88	74				
86	82	84	75	70	78	86	82					134	136	130	145	132	132	112	132					88	92	86	90	79	82	76	76				
78	84	78	74	74	76	74	84					116	135	149	121	116	135	126	115					88	90	82	80	88	90	96	81				
82	78	84	75	72	74	72	76					149	136	132	122	132	132	130	129					96	92	72	66	72	75	85	76				
84	76	78	76	76	72	76	82	84				117	118	120	130	120	116	123	121	118				72	78	74	85	76	77	88	86	69			
82	78	86	78	89	86	82	84					122	132	124	128	124	121	119	115					88	88	84	81	84	74	76	70				
84	86	78	86	87	82	78	86					137	133	142	119	123	120	135	134					79	85	96	76	81	82	90	88				
85	82	84	82	84	86	84	78					122	130	130	118	122	122	132	120					72	80	72	78	76	74	70	74				
78	84	86	84	82	85	82	84					138	137	133	132	122	134	122	124					88	96	85	88	88	88	81	84				
84	78	81	78	72	78	72	76					128	122	134	121	122	124	132	134					81	88	88	74	88	84	86	88				
78	86	76	83	78	76	78	82					122	132	124	126	119	124	130	130					86	72	84	80	76	84	72	85				
89	83	84	82	84	82	86	84					120	130	134	120	122	124	122	130					74	80	82	86	72	82	81	68				
82	75	76	78	72	74	79	82					125	128	130	114	116	118	125	100					84	75	81	87	80	78	84	60				
78	76	86	84	78	72	73	78					118	130	132	118	126	126	118	128					73	80	76	72	83	80	74	77				
86	78	86	82	84	78	76	72					134	132	128	124	121	122	130	130					82	72	81	85	81	88	81	68				
84	82	84	86	90	85	78	82					134	132	130	111	104	122	128	118					85	72	81	68	80	88	88	72				
76	78	86	82	86	82	84	86					120	127	120	126	122	117	124	130					73	89	73	80	88	73	85	64				
84	82	86	83	84	76	78	72					105	120	134	130	130	127	130	122					85	68	68	68	86	89	77	80				
78	72	76	82	86	82	76	82					132	122	128	117	130	120	126	116					85	87	77	73	85	73	85	88				
72	76	74	84	78	83	87	86	88				120	133	126	122	125	120	120	130	132				73	86	80	88	81	70	86	64	79			
76	78	76	86	83	82	85	88					130	132	130	121	122	123	120	121					78	68	68	86	66	73	68	78				
73	78	82	81	75	76	82	84					120	126	131	136	124	121	126	123					85	74	80	76	85	78	70	73				
88	74	84	88	83	82	86	83					122	126	129	128	130	121	128	132					78	81	84	75	81	78	83	84				
78	72	78	80	86	89	78	79					131	133	134	136	128	124	124	140					80	75	76	76	86	84	64	80				

INTRAOPERATIVE MEAN BLOOD PRESSURE IN mmHg												INTRA OPERATIVE SURFACE TEMPERATURE												INTRA OPERATIVE OT TEPERATURE											
15	30	45	60	75	90	105	120	135	150	165	180	15	30	45	60	75	90	105	120	135	150	165	180	15	30	45	60	75	90	105	120	135	150	165	180
91	90	86	99	90	91	85	81					36.5	36.3	36.4	36.3	34.6	36.4	36.3	36.2					22.2	22.4	22.4	23.2	22.5	22.6	22.7	22.8				
91	93	90	86	86	80	85	79					36.6	36.5	36.4	36.2	35.8	36.1	36.2	36.1					22.8	22.8	22.5	22.4	22.6	22.4	22.4	22.8				
103	95	108	81	81	87	95	76					36.7	36.5	36.4	36.2	36.6	36.8	36.7	36.7					22.3	23.2	22.4	23.2	22.8	22.5	23	22.4				
95	112	112	86	86	96	96	105					36.5	36.7	36.5	36.8	36.1	36.2	36.8	36.8					22.5	22.7	22.6	22.5	22.3	22.7	22.5	22.5				
112	103	92	91	91	96	103	90					36.4	36.5	36.8	36.5	36.7	36.5	36.6	36.4					22.4	22.6	22.7	22.4	22.2	22.6	22.4	22.6				
93	85	86	95	95	94	92	96					36.8	36.5	36.6	36.6	36.4	36.8	36.7	36.2					22.7	22.4	22.6	22.6	23.2	22.8	22	22.7				
93	100	88	100	92	93	93	95					36.6	36.4	36.7	36.5	36.6	36.2	36.6	36.7					22.8	22.3	22.2	22.3	22.7	22.5	22.6	22.3				
93	103	95	114	103	100	90	90					36.5	36.6	36.8	36.8	36.1	36.4	36.8	36.5					22.9	22.5	22.4	22.5	22.3	22.2	22.7	22.9				
93	105	99	103	93	105	107	92					36.6	36.4	36.5	36.2	36.6	36.4	36.2	36.8					22.5	22.2	22.5	22.6	22.7	22.6	22.7	22.4				
96	103	96	77	96	95	94	86					36.6	36.4	36.8	36.6	36.2	36.8	36.1	36.7					22.4	22.7	22.8	22.3	22.2	22.3	22.3	22.6				
83	98	89	100	96	86	102	104	85				36.5	36.4	36.4	36.1	36.2	36.2	35.8	36.8	36.2				22.3	22.4	22.6	22.5	22.6	22.4	22.6	22.4	22.8			
99	96	101	95	101	96	88	90					36.8	36.4	36.4	36.6	36.5	36.7	36.2	36.6					22.6	22.2	23.2	22.4	22.8	22.5	22.5	22.3				
89	98	110	88	89	96	92	103					36.6	36.5	36.6	36.2	36.1	36.2	36.1	36.7					22.7	22.5	22.3	22.5	22.4	22.6	22.3	22.8				
88	96	90	91	89	90	90	93					36.7	36.5	36.8	36.2	36.4	36.5	36.8	36.2					22.8	22.3	22.6	22.2	22.3	22.7	22.4	23.2				
90	89	98	96	99	103	94	101					36.5	36.4	36.8	36.8	36.4	36.2	36.8	36.6					22.9	22.4	22.8	22.3	22.4	22.6	22.8	23.4				
95	95	103	96	99	101	96	95					36.6	36.4	36.4	36.7	35.8	36.6	36.4	36.4					22.3	22.9	22.7	22.6	22.8	22.2	22.7	22.5				
98	91	101	88	88	101	90	96					36.5	36.6	36.4	36.2	36.8	36.1	36.7	36.8					22.4	22.8	22.5	22.4	23.2	22.4	22.6	22.6				
93	96	99	99	88	96	94	88					36.7	36.3	36.5	36.4	36.2	36.5	36.6	36.2					22.5	22.7	22.3	22.5	23.4	22.5	22.3	22.5				
95	88	95	91	92	98	95	71					36.7	36.5	36.4	36.6	36.4	36.6	36.2	36.4					22.3	22.6	22.4	22.8	22.9	22.4	22.5	22.6				
98	96	96	78	70	88	98	90					36.4	36.5	36.4	36.2	36.8	36.4	35.9	36.8					23.2	22.3	22.5	22.6	22.5	23.2	22.4	22.2				
99	91	95	95	95	99	95	88					36.5	36.4	36.4	36.7	36.5	36.5	36.5	36.8					22.5	22.4	22.3	22.2	22.3	23.4	23.2	22.6				
103	91	95	79	88	99	103	88					36.5	36.6	36.4	36.2	36.2	36.5	36.4	36.6					22.2	22.3	22.5	22.4	22.5	22.4	22.9	22.2				
88	100	80	95	99	87	98	95					36.6	36.3	36.5	36.4	36.2	36.8	36.5	36.2					22.4	22.6	22.7	22.6	22.2	22.3	22.7	22.4				
78	88	85	90	95	100	100	94					36.5	36.5	36.4	36.2	36.8	36.5	36.2	36.1					22.2	22.8	22.5	22.8	22.5	22.2	22.8	22.6				
96	99	96	87	94	86	96	93					36.8	36.5	36.4	36.6	36.3	36.4	36.8	36.8					23.2	22.6	22.6	22.6	22.6	22.3	22.6	22.4				
99	100	95	99	91	88	88	95	93				36.6	36.7	36.5	36.8	36.5	36.2	36.6	36.7	36.4				22.6	22.4	22.5	22.7	22.6	22.2	22.3	22.5	22.4			
88	96	90	94	77	90	92	90					36.7	36.5	36.6	36.2	36.7	36.2	36.4	36.8					22.5	22.2	22.4	22.4	22.5	22.4	22.5	22.3				
89	90	90	96	95	90	96	97					36.5	36.5	36.5	36.2	36.4	36.7	36.6	36.2					22.7	22.5	22.3	22.2	22.3	22.6	22.4	22.7				
93	90	96	88	95	90	109	96					36.6	36.4	36.7	36.5	36.8	36.2	36.8	36.6					22.5	22.6	22.5	22.4	22.5	22.8	23.2	22.3				
90	100	96	96	100	101	82	100					36.7	36.6	35.8	35.9	36.1	36.4	35.8	36.8					22.5	22.4	22.2	22.5	22.3	22.6	22.3	22.4				

INTRA OPERATIVE CORE TEMPERATURE												POST OPERATIVE HEART RATE/MIN		POST OPERATIVE SBP IN mmHg		POST OPERTIVE DBP IN mmHg		POST OPERATIVE MAP IN mmHg		POST OPERATIVE SPO2%		POST OP ROOM TEMP		POST OPERATIVE CORE TEMPERATURE	
15	30	45	60	75	90	105	120	135	150	165	180	15	30	15	30	15	30	15	30	15	30	15	30	15	30
36.6	36.6	36.7	36.5	36.6	36.6	36.6	36.7					86	88	132	126	80	74	97	91	99	99	22.4	22.8	36.6	36.7
36.5	36.5	36.6	36.6	36.6	36.5	36.6	36.6					88	90	134	128	72	76	99	90	99	99	22.8	22.6	36.5	36.6
36.7	36.7	36.5	36.7	36.7	36.7	36.7	36.5					96	82	136	134	82	80	100	98	99	99	22.2	23.2	36.7	36.5
36.8	36.7	36.8	36.8	36.5	36.7	36.5	36.8					84	78	138	130	84	78	102	96	99	99	22.6	22.6	36.7	36.8
36.8	36.8	36.7	36.7	36.6	36.6	36.6	36.7					82	86	132	126	80	84	97	98	99	99	22.8	22.4	36.8	36.7
36.6	36.5	36.6	36.5	36.6	36.5	36.6	36.6					92	90	138	132	84	70	102	87	99	99	21.4	22.6	36.5	36.6
36.6	36.6	36.5	36.6	36.6	36.7	36.6	36.5					86	84	136	124	80	72	98	99	99	99	22.5	22.5	36.6	36.5
36.5	36.5	36.6	36.5	36.5	36.6	36.5	36.6					78	83	132	122	80	72	94	88	99	99	21.9	22.3	36.5	36.6
36.7	36.6	36.5	36.6	36.6	36.7	36.6	36.5					82	79	128	132	78	82	94	96	99	99	21.7	22.8	36.6	36.5
36.9	36.7	367	36.6	36.6	36.8	36.6	367					86	84	130	126	82	72	98	90	99	99	22.8	22.3	36.7	367
36.5	36.6	36.6	36.7	36.5	36.6	36.5	36.6	36.6				88	87	126	128	70	82	98	97	99	99	22	22.4	36.6	36.6
36.6	36.7	36.7	36.7	36.8	36.7	36.8	36.7					84	92	136	126	78	76	94	92	99	99	22.8	22.3	36.7	36.7
36.6	36.6	36.6	36.6	36.6	36.5	36.6	36.6					78	86	134	118	80	80	97	92	99	99	22.6	22.2	36.6	36.6
36.7	36.7	36.7	36.7	36.7	36.6	36.7	36.7					90	88	122	124	72	78	88	91	99	99	22.4	21.2	36.7	36.7
36.5	36.8	36.8	36.8	36.5	36.7	36.5	36.8					95	84	128	119	75	80	91	93	99	99	22.4	22.9	36.8	36.8
36.7	36.6	36.7	36.5	36.6	36.6	36.6	36.7					97	78	138	134	80	70	99	86	99	99	21.8	22.5	36.6	36.7
36.7	36.5	36.6	36.6	36.5	36.6	36.5	36.6					78	90	132	124	70	78	87	92	99	99	22.7	22.6	36.5	36.6
36.6	36.7	36.5	36.7	36.7	36.7	36.7	36.5					84	95	128	130	76	84	93	99	99	99	22.2	22.7	36.7	36.5
36.4	36.7	36.8	36.8	36.7	36.5	36.7	36.8					86	97	126	132	80	78	95	96	99	99	22.3	22.5	36.7	36.8
36.6	36.8	36.7	36.7	36.6	36.6	36.6	36.7					78	78	130	134	80	80	96	96	99	99	22	22.3	36.8	36.7
36.7	36.5	36.6	36.5	36.5	36.6	36.5	36.6					79	84	132	128	76	78	96	94	99	99	22.4	22.7	36.5	36.6
36.8	36.6	36.5	36.6	36.7	36.6	36.7	36.5					92	86	136	126	83	80	99	95	99	99	22.7	22.6	36.6	36.5
36.5	36.5	36.6	36.5	36.6	36.5	36.6	36.6					98	78	133	128	78	86	97	101	99	99	22.6	22.8	36.5	36.6
36.6	36.6	36.5	36.6	36.7	36.6	36.7	36.5					94	79	135	122	75	82	95	96	99	99	22.5	22.5	36.6	36.5
36.8	36.7	367	36.6	36.8	36.6	36.8	367					92	92	128	126	80	80	96	95	99	99	22.8	22.3	36.7	367
36.7	36.6	36.6	36.7	36.6	36.5	36.6	36.6	36.7				86	98	136	130	82	80	99	96	99	99	22.5	22.5	36.6	36.6
36.6	36.7	36.7	36.7	36.7	36.8	36.7	36.7					90	94	134	132	75	82	94	98	99	99	22.2	22.3	36.7	36.7
36.5	36.6	36.6	36.6	36.5	36.6	36.5	36.6					96	92	128	132	80	80	99	97	99	99	22.5	22.5	36.6	36.6
36.7	36.7	36.7	36.7	36.6	36.7	36.6	36.7					90	96	128	120	85	72	99	88	99	99	22.8	22.3	36.7	36.7
36.6	36.8	36.8	36.8	36.7	36.5	36.7	36.8					90	94	134	132	75	82	94	98	99	99	22	22.4	36.8	36.8

POSTOP SURFACE TEMP		POST OPERATIVE SHIVERING SCORE						COMLICATION				
15	30	5	10	15	20	25	30	NAUSEA	VOMITING	TACHYCARDIA	HYPOTENSION	DESATURATION
36.8	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.7	36.5	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.6	36.7	0	;	0	0	0	0	NO	NO	NO	NO	NO
36.5	36.7	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.6	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.5	36.5	1	1	1	1	1	1	NO	NO	NO	NO	NO
36.7	36.7	0	0	0	0	0	0	NO	NO	NO	NO	NO
36.6	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.7	36.7	2	2	2	2	2	2	NO	NO	NO	NO	NO
36.6	36.8	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.7	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.8	36.7	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.7	36.5	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.6	36.6	0	0	0	0	0	0	NO	NO	NO	NO	NO
36.5	36.7	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.8	36.6	0	0	0	0	0	0	NO	NO	NO	NO	NO
36.7	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.6	36.7	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.5	36.5	0	0	0	0	0	0	NO	NO	NO	NO	NO
36.6	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.5	36.6	2	2	2	2	2	2	NO	NO	NO	NO	NO
367	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.6	36.5	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.7	36.6	0	0	0	0	0	0	NO	NO	NO	NO	NO
36.6	36.6	3	3	3	3	3	3	NO	NO	NO	NO	NO
36.7	36.5	0	0	0	0	0	0	NO	NO	NO	NO	NO
36.8	36.8	3	3	3	3	3	3	NO	NO	NO	NO	NO
	36.6	0	0	0	0	0	0	NO	NO	NO	NO	NO
	36.7	2	2	2	2	2	2	NO	NO	NO	NO	NO
	36.5	3	3	3	3	3	3	NO	NO	NO	NO	NO

PATIENT CONSENT FORM

STUDY TITLE:

A Prospective, Randomized Comparative study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine for the Prevention of postoperative Shivering in Patients Undergoing Elective thyroid surgeries.

STUDY CENTER:

Institute of Anaesthesiology and Critical Care,
Madras Medical college,
Chennai- 600003.

Participant name : **Age:** **Sex:**

I.P.No:

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction. I have been explained about the pitfall in the procedure. I have been explained about the safety, advantage and disadvantage of the technique.

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason.

I understand that investigator, regulatory authorities and the ethical committee will not need my permission to look at my health records both in respect to current study and any further research that may be conducted in relation to it, even if I withdraw from the study. I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

Time :

Date : **Signature / Thumb impression of patient**

Place : **Patient name:**

Signature of the investigator: **Name of the investigator:**

INFORMATION TO PARTICIPANTS

Investigator:

Name of the Participant:

Title:

A Prospective, Randomized Comparative Study to Compare the Effectiveness of Prophylactic Granisetron versus Pethidine for Prevention of Postoperative Shivering in Patients Undergoing Elective Thyrod Surgeries.

You are invited to take part in this research study. We have got approval from the Institutional Ethical Committee. You are asked to participate since you satisfy the eligibility criteria. We want to compare the effectiveness of prophylactic Granisetron versus Pethidine for prevention of postoperative shivering in patients undergoing elective breast surgeries.

Purpose of Research:

For thyroid surgeries, prophylactic inj.Granisetron or inj,Pethidine iv given before induction then patient anaesthetized This study is done to compare effectiveness in prevention of postoperative shivering in patients undergoing elective thyroid surgery with respect to,

1. Base line, Intra operative and post operative temperature ,BP,PR and SPO2

2. Post operative shivering score for shivering

The Study Design

All the patients in the study will be divided into three groups:

Group1- prophylactic inj,Granisetron

Group2- Prophylactic inj,Pethidine

Group3. Placebo saline

Drugs Will be Given IV Before Induction And All patients will be given general anaesthesia.

Benefits:

Both Drugs Prevents Postoperative Shivering, Granisetron also Prevents Vomiting.

Discomforts and Risks:

Nausea and Vomiting treated by inj.metoclopramide 10mg.

Hypotension, Tachycardia may occur – emergency drugs will be readily available.

This intervention has been shown to be well tolerated by previous studies. But if you do not want to participate, you will be provided with an alternative setting of standard treatment. Your safety is our prime concern.

Time:

Place:

Date:

Name of the Investigator : Signature / Thumb impression o of the patient

Name of the Investigator : Name of the patient:

PROFORMA

Date: ……. Drug:
Roll No.:

Name: ……

Age: Sex: …….. Wt: Kg, Ht: …….Cms, IP No:

Diagnosis: **Surgical Procedure :**

Pre operative Assessment : General Anaethesia , ASA I / II

- H/O Any Co-morbid illness **:**
- H/O Documented Difficult Airway **:**
- H/O previous surgeries

Examination:

CVS:

RS:

ABDOMEN:

CNS:

Measures of Study Outcome:

Postoperative Shivering and Vitals for 30Minutes

Shivering Scale:

Grade:

0- No shivering
1- Piloerection ,no visible shivering
2- Muscular activity in only one group
3- Muscular activity in more than one group but not generalised
4- Shivering generalised involving whole body

Time	SBP mmHg	DBP mmHg	MAP mmHg	SPO2 %	PR	Core Temp°C	OT Temp°C	Surface Temp°C	Shivering score
5									
10 15									
20									
25									
30									
35									
40									
45									
50									
55									
60									
65									
70									
75									
80									
85									
90									
95 100									
105									
110									
115									
120									
125									
130									
135									
140									
145									
150									
155									
160									
165									
170									
175									
180									

Post operative period

Time	SBP mmHg	DBP mmHg	MAP mmHg	SPO2 %	PR	Core Temp°C	OT Temp°C	Surface Temp°C	Shivering score
15									
30									

Complications: Nausea / vomiting Tachycardia / Bradycardia/Hypotension /Desaturation

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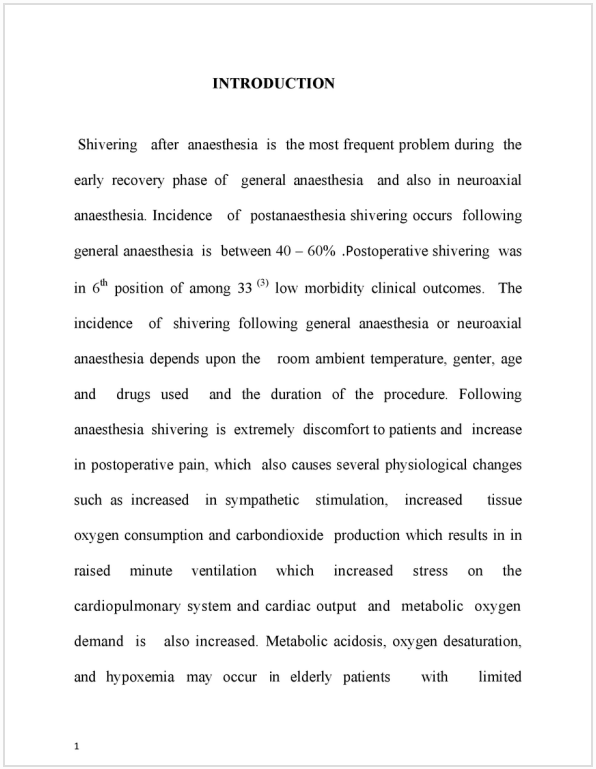

INTRODUCTION

Shivering after anaesthesia is the most frequent problem during the early recovery phase of general anaesthesia and also in neuroaxial anaesthesia. Incidence of postanaesthesia shivering occurs following general anaesthesia is between 40 – 60% .Postoperative shivering was in 6th position of among 33 [3] low morbidity clinical outcomes. The incidence of shivering following general anaesthesia or neuroaxial anaesthesia depends upon the room ambient temperature, genter, age and drugs used and the duration of the procedure. Following anaesthesia shivering is extremely discomfort to patients and increase in postoperative pain, which also causes several physiological changes such as increased in sympathetic stimulation, increased tissue oxygen consumption and carbondioxide production which results in in raised minute ventilation which increased stress on the cardiopulmonary system and cardiac output and metabolic oxygen demand is also increased. Metabolic acidosis, oxygen desaturation, and hypoxemia may occur in elderly patients with limited

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